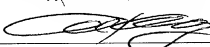


JC20 Rec'd PCT/PTO SEP 28 2001

GAMBROFORM PTO 1390		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER	
TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371				GAMBRO-257	
INTERNATIONAL APPLICATION NO. PCT/SE00/00615		INTERNATIONAL FILING DATES 30 MARCH 2000		U.S. APPLICATION NO. (if known, see 37 CFR 1.55) 09/937990	
				PRIORITY DATE CLAIMED 30 MARCH 1999	
TITLE OF INVENTION METHOD, APPARATUS AND COMPONENTS OF DIALYSIS SYSTEM					
APPLICANT(S) FOR DO/EO/US Olof JANSSON, et al.					
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:					
1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.					
2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.					
3. <input checked="" type="checkbox"/> This is an express request to promptly begin national examination procedures (35 U.S.C. 371 (f)).					
4. <input checked="" type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).					
5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371 (c)(2))					
a. <input type="checkbox"/> is attached hereto (required only if not transmitted by the International Bureau).					
b. <input checked="" type="checkbox"/> has been communicated by the International Bureau.					
c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).					
6. <input type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371 (c)(2)).					
7. <input checked="" type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3))					
a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau).					
b. <input type="checkbox"/> have been communicated by the International Bureau.					
c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.					
d. <input checked="" type="checkbox"/> have not been made and will not be made.					
8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).					
9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)). (Unexecuted)					
10. <input type="checkbox"/> An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).					
Items 11. to 16. below concern document(s) or information included:					
11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98. w/PTO-1449, <u>22</u> references					
12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 & 3.31 is included.					
13. <input checked="" type="checkbox"/> A FIRST preliminary amendment.					
<input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment.					
14. <input checked="" type="checkbox"/> A substitute specification.					
15. <input type="checkbox"/> A change of power of attorney and/or address letter					
16. <input checked="" type="checkbox"/> Other items or information:					
-Substitute Abstract					
-Marked-up copy of the specification					
-Copy of International Application as published					
-Copy of International Preliminary Examination Report					
-Twenty-Six (26) Sheets Formal Drawings					

EXPRESS MAIL LABEL NO. EL804522432US
DATE: September 28, 2001

JC09 Rec'd PCT/PTO 2 8 SEP 2001

U.S. APPLICATION NO. (if known, see 37 CFR 1.5) <div style="font-size: 1.2em; font-weight: bold; margin-top: 5px;">09/937990</div>	INTERNATIONAL APPLICATION NO. PCT/SE00/00615	ATTORNEY'S DOCKET NUMBER GAMBRO-257
17. <input checked="" type="checkbox"/> The following fees are submitted: <div style="margin-top: 5px;"> BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)): <input checked="" type="checkbox"/> Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$1,000.00 <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$860.00 <input type="checkbox"/> International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$710.00 <input type="checkbox"/> International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$690.00 <input type="checkbox"/> International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) \$100.00 </div>		CALCULATIONS PTO USE ONLY <div style="border: 1px solid black; height: 100px; width: 100%;"></div>
ENTER APPROPRIATE BASIC FEE AMOUNT =		1,000.00
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (e)).		
CLAIMS	NUMBER FILED	NUMBER EXTRA
Total claims	*135 - 20 =	115
Independent claims	30 - 3 =	27
MULTIPLE DEPENDENT CLAIM(s) (if applicable)		+ \$270.00
TOTAL OF ABOVE CALCULATIONS =		5,230.00
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.		
SUBTOTAL =		5,230.00
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492 (f)). +		
TOTAL NATIONAL FEE =		5,230.00
Fee for recording the enclosed assignment (37 CFR 1.21 (h)). Assignment must be accompanied by appropriate cover sheet (37 CFR 3.28, 3.31) + (\$40.00 per property).		
TOTAL FEES ENCLOSED =		5,230.00
*As In Preliminary Amendment		Amount to be: Refunded
		Charged
a. <input type="checkbox"/> A check in the amount of _____ to cover the above fees is enclosed. b. <input checked="" type="checkbox"/> Please charge my Deposit Account No. 12-1095 in the amount of \$5,230.00 to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required or credit any overpayment to my Deposit Account No. 12-1095. A duplicate copy of this sheet is enclosed.		
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.		
SEND ALL CORRESPONDENCE TO:		
<div style="display: flex; justify-content: space-between; align-items: flex-end;"> <div style="width: 45%;"> Lerner, David, Littenberg, Krumholz & Mentlik, LLP 600 South Avenue West Westfield, NJ 07090 Telephone 908 654-5000 Facsimile 908 654-7866 </div> <div style="width: 45%; text-align: right;"> <div style="text-align: center;">  Signature </div> <div style="margin-top: 10px;"> ARNOLD H. KRUMHOLZ Name 25,428 Registration Number </div> </div> </div>		



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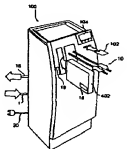
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(54) Title: METHOD, APPARATUS AND COMPONENTS OF DIALYSIS SYSTEM

(57) Abstract

The apparatus (100) for the preparation of peritoneal dialysis fluid comprises a water preparation module (200) which purifies tap water and supplies the purified water to a thermal control and sterilisation module (300). The thermal control and sterilisation module (300) passes the purified water to a concentrate mixing module (400), which mixes the purified water with concentrated components of the dialysis fluid from a disposable concentrate container (402) to produce the peritoneal dialysis fluid. At least some of the concentrated components of the dialysis fluid are in powdered form. The peritoneal dialysis fluid is passed from the concentrate mixing module (400) back to the thermal control and sterilisation module (300) where it is sterilised in an on-line autoclave, before being passed to a cycler and sterilisable connector module (600) for administration to the patient (50). The apparatus has the advantage that the peritoneal dialysis fluid is prepared on-line at a treatment location, such as a patient's bedroom, to a prescription specific to the patient.



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PATENT
GAMBRO 3.3-257

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of :
Olof JANSSON et al. :
: Group Art Unit:
International Application No. :
PCT/SE00/00615 : Examiner:
: Date: September 28, 2001
International Filing Date: :
30 March 2000 :
: For: METHOD, APPARATUS AND
COMPONENTS OF DIALYSIS SYSTEM :
X

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Preliminary to initiation of the prosecution of the above-identified pending U.S. patent application, the following amendments and remarks are respectfully submitted.

IN THE ABSTRACT

Please delete the Abstract as filed and substitute therefor the attached revised Abstract.

IN THE SPECIFICATION

Please amend the Specification in accordance with the attached revised Specification.

IN THE CLAIMS

Please cancel claims 1-143 and add new claims 144-279.

144. (NEW) A container for use in the preparation of a peritoneal dialysis fluid, said container comprising a plurality of chambers, and a corresponding plurality of concentrates for said peritoneal dialysis fluid, at least one of said plurality of concentrates in at least one of said chambers comprising a concentrate in the form of a powder.

145. (NEW) The container of claim 144 wherein at least one of said plurality of chambers has a volume whereby at least

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one of said plurality of concentrates in said at least one of said plurality of chambers is present in an amount which is incapable of being fully dissolved when said at least one of said plurality of chambers is filled with liquid.

146. (NEW) The container of claim 144 wherein at least one of said plurality of concentrates in at least one of said plurality of chambers comprises powdered glucose and at least one other of said plurality of concentrates in at least one other of said plurality of chambers comprises an inorganic salt in substantially dry form.

147. (NEW) A container for use in the preparation of a dialysis fluid, said container comprising a plurality of chambers, a cleaning agent disposed in at least one of said plurality of chambers, and a powdered inorganic salt disposed in at least one other of said plurality of chambers.

148. (NEW) A container for use in the preparation of a dialysis fluid, said container comprising a plurality of chambers, a first amount of a first inorganic salt disposed in at least one of said plurality of chambers, and a second amount of a second inorganic salt different from said first inorganic salt disposed in another of said plurality of chambers, said at least one of said plurality of chambers having a first volume and said another of said plurality of chambers having a second volume, whereby when said first and second inorganic salts are prepared by filling said at least one and said another of said plurality of chambers with a liquid to provide solutions of said first and second inorganic salts, said solutions of said first and second inorganic salts have characteristically different conductivities.

149. (NEW) A container for use in the preparation of a dialysis fluid, said container comprising a plurality of distinct chambers, a corresponding plurality of concentrate components of said dialysis fluid in said plurality of distinct chambers, and a corresponding plurality of connectors for each of said plurality of distinct chambers, each of said plurality of connectors including at least two separate fluid channels so as to provide

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for simultaneous inflow and outflow from each of said plurality of distinct chambers.

150. (NEW) The container of claim 149 wherein said at least two separate fluid channels comprise first and second concentric fluid channels.

151. (NEW) The container of claim 149 wherein at least one of said plurality of distinct chambers includes a plurality of said connectors, including a first connector comprising a plurality of first fluid channels comprising said at least two separate fluid channels and a second connector including a second fluid channel.

152. (NEW) The container of claim 149 wherein said plurality of distinct chambers include an upper region and a lower region, said plurality of connectors being disposed at said lower regions of said plurality of distinct chambers, and wherein one of said at least two separate fluid channels and at least one of said plurality of connectors associated with at least one of said plurality of distinct chambers includes a channel portion extending to said upper region of said at least one of said plurality of distinct chambers.

153. (NEW) The container of claim 149 including a diffuser disposed in one of said at least two separate fluid channels in at least one of said plurality of connectors associated with at least one of said plurality of distinct chambers whereby an inflow of liquid into said at least one of said plurality of distinct chambers can be diffused.

154. (NEW) The container of claim 149 wherein said plurality of connectors are aligned along a predetermined linear axis.

155. (NEW) The claimer of claim 154 wherein said container includes a central axis, and said predetermined linear axis is offset from said central axis.

156. (NEW) A container for priming powdered glucose at a predetermined patient location, said container including an upper region and a lower region, said powdered glucose, an inlet port in said lower region for receiving a supply of water to

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dissolve said powdered glucose, and a diffuser associated with said inlet port for diffusing said flow of water into said powdered glucose.

157. (NEW) A container for use in connection with a dialysis fluid, said container comprising a plurality of distinct chambers, and a corresponding plurality of connectors for each of said plurality of distinct chambers, each of said plurality of connectors being aligned along a predetermined linear axis.

158. (NEW) A universal container for use in connection with a dialysis solution, said universal container including a plurality of compartments, a corresponding plurality of predetermined amounts of chemical components in each of said plurality of compartments, wherein upon combination with a liquid said plurality of chemical components can provide a plurality of different formulations of said dialysis solution for a corresponding plurality of patient requirements, and at least one port associated with said plurality of compartments for providing fluid communication with a dialysis treatment system.

159. (NEW) The universal container of claim 158 wherein said plurality of compartments comprises five compartments, each of said five compartments including one of said plurality of predetermined amounts of chemical components, said at least one port comprising five ports, each of said five ports being in fluid communication with one of said five compartments.

160. (NEW) The universal container of claim 158 wherein said plurality of predetermined amounts of said chemical components comprises a sufficient amount of said chemical component whereby a substantial amount of chemical component remains in said container after preparation of said dialysis solution and infusion into said patient.

161. (NEW) A container for use in the preparation of a dialysis fluid, said container including a first compartment, calcium chloride in said first compartment, a second compartment, magnesium chloride in said second compartment, a third compartment, sodium chloride in said third compartment, a fourth

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compartment, a cleaning agent in said fourth compartment, a fifth compartment, sodium bicarbonate in said fifth compartment, a sixth compartment, glucose in said sixth compartment, a plurality of ports associated with each of said first, second, third, fourth, fifth and sixth compartments whereby said plurality of ports can be connected to a dialysis treatment unit for preparation of said dialysis solution at a patient treatment location.

162. (NEW) The container of claim 161 wherein at least one of said calcium chloride, magnesium chloride, sodium chloride, cleaning agent, sodium bicarbonate and glucose is in substantially dry form, and wherein one of said plurality of ports associated with said compartment containing said at least one of said calcium chloride, magnesium chloride, sodium chloride, cleaning agent, sodium bicarbonate and glucose includes inlet means for receiving liquid for mixing with said substantially dry form of said calcium chloride, magnesium chloride, sodium chloride, cleaning agent, sodium bicarbonate or glucose to form a solution thereof in said compartment.

163. (NEW) The container of claim 161 including a seventh compartment, and lactic acid contained in said seventh compartment.

164. (NEW) The container of claim 161 including readable indicia associated with said container, whereby said readable indicia can be read by said dialysis treatment unit.

165. (NEW) A container for use in connection with dialysis comprising a plurality of compartments including a first compartment, an ionic component of a dialysis solution disposed in said first compartment, a second compartment, and a cleaning agent or a precursor of said cleaning agent for cleaning a flow path in a dialysis system disposed in said second compartment, said container including a plurality of ports whereby said first and second compartments can be placed in fluid communication with said dialysis system.

166. (NEW) The container of claim 165 wherein said ionic component comprises calcium chloride, and including a third

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compartment, magnesium chloride disposed in said third compartment, a fourth compartment, sodium chloride disposed in said fourth compartment, a fifth compartment, sodium bicarbonate disposed in said fifth compartment, a sixth compartment, and glucose disposed in said sixth compartment.

167. (NEW) The container of claim 166 including a seventh compartment, and lactic acid disposed in said seventh compartment.

168. (NEW) A container including a surface having a longitudinal axis for use in connection with dialysis comprising a plurality of compartments, a corresponding plurality of chemical compositions in each of said plurality of compartments, and a plurality of fluid ports in fluid communication with each of said plurality of compartments, whereby each of said plurality of compartments can be placed in fluid communication with a dialysis system, at least one of said plurality of ports being disposed along said surface of said container asymmetrically with respect to said longitudinal axis of said surface of said container.

169. (NEW) The container of claim 168 wherein each of said plurality of ports includes a longitudinal axis, and said plurality of longitudinal axes of each of said plurality of ports are aligned.

170. (NEW) The container of claim 168 including a plurality of septums associated with each of said plurality of ports, each of said plurality of septums being pierceable by a respective connector associated with said dialysis system.

171. (NEW) The container of claim 168 including at least a first plurality of flanges associated with said plurality of ports, said at least a first plurality of flanges engageable with a mount associated with said dialysis system.

172. (NEW) The container of claim 168 wherein each of said plurality of ports includes a free end, each of said free ends of said plurality of ports being coplanar.

173. (NEW) The container of claim 168 wherein said plurality of compartments includes a first compartment, said

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chemical component in said first compartment comprising calcium chloride, a second compartment, said chemical component in said second compartment comprising magnesium chloride, a third compartment, said chemical component in said third compartment comprising sodium chloride, a fourth compartment, said chemical component in said fourth compartment comprising a cleaning agent, a fifth compartment, said chemical component in said fifth compartment comprising sodium bicarbonate, and a sixth compartment, said chemical component in said sixth compartment comprising glucose.

174. (NEW) The container of claim 173 including a seventh compartment, said chemical component in said seventh compartment comprising lactic acid.

175. (NEW) The container of claim 168 including a barcode on said surface of said container, whereby said barcode can be read by a barcode reader associated with said dialysis system.

176. (NEW) The container of claim 168 including a plurality of vent tubes associated with said plurality of compartments.

177. (NEW) The container of claim 168 including a first flow conduit associated with at least one of said plurality of ports for passing air into at least one of said compartments, and a second flow conduit associated with at least another one of said ports for fluid communication with at least one of said plurality of compartments.

178. (NEW) A container for use in connection with dialysis including a plurality of compartments, a corresponding plurality of chemical components in each of said plurality of compartments, a plurality of ports associated with each of said plurality of compartments for fluid communication with a dialysis system, and readable indicia disposed on said container, said readable indicia being indicative of the contents of said plurality of compartments, whereby said readable indicia can be recognized by said dialysis system.

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179. (NEW) The container of claim 178 wherein said readable indicia comprises a barcode symbol.

180. (NEW) The container of claim 178 wherein said readable indicia includes patient prescription information.

181. (NEW) The container of claim 178 wherein said plurality of compartments includes a first compartment, said chemical component in said first compartment comprising calcium chloride, a second compartment, said chemical component in said second compartment comprising magnesium chloride, a third compartment, said chemical component in said third compartment comprising sodium chloride, a fourth compartment, said chemical component in said fourth compartment comprising a cleaning agent, a fifth compartment, said chemical component in said fifth compartment comprising sodium bicarbonate, and a sixth compartment, said chemical component in said sixth compartment comprising glucose.

182. (NEW) The container of claim 181 including a seventh compartment, said chemical component in said seventh compartment comprising lactic acid.

183. (NEW) A container for use in connection with dialysis comprising a first compartment including a first air vent channel, a first fluid channel and a first port in fluid communication with said first air vent channel and said first fluid channel, a second compartment including a second air vent channel, a second fluid channel, and a second port in fluid communication with said second air vent channel and said second fluid channel, a third compartment including a third air vent channel, a third fluid channel, and a third port in fluid communication with said third air vent channel and said third fluid channel, a fourth compartment including a fourth air vent channel, a first fourth port in fluid communication with said fourth air vent channel, a fluid input channel, and a diffuser in fluid communication with said fluid input channel, a fluid output channel, a second fourth port in fluid communication with said fluid input channel and said fluid output channel, and a glucose filter in fluid communication with said fluid output channel, a

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fifth compartment including a fifth air vent channel, a fifth fluid channel, and a fifth port in fluid communication with said fifth air vent channel and said fifth fluid channel, a sixth compartment including a first air vent/fluid flow channel, a first fluid input/output channel and a sixth port in fluid communication with said first air vent/fluid flow channel and said first fluid input/output channel, a seventh compartment including a second air vent/fluid flow channel, a second fluid input/output channel, and a seventh port in fluid communication with said second air vent/fluid flow channel and said second fluid input/output channel, said plurality of compartments being sized to contain respective amounts of said components of said dialysis solution, said ports being placeable in fluid communication with a dialysis processing machine.

184. (NEW) Apparatus for the production of peritoneal dialysis solution comprising a plurality of chambers, a corresponding plurality of concentrates of constituents of said peritoneal dialysis solution, a mixer for mixing said corresponding plurality of concentrates with a predetermined liquid to produce said peritoneal dialysis solution, a sterilizer for sterilizing at least one of said peritoneal dialysis solution and said predetermined liquid, and a patient connector for supplying said peritoneal dialysis solution to the peritoneal cavity of said patient, at least one of said corresponding plurality of concentrates comprising a concentrate in substantially dry form, whereby in use said concentrate in said substantially dry form can be at least partially dissolved to be included in said peritoneal dialysis solution.

185. (NEW) The apparatus of claim 184 wherein at least one other of said corresponding plurality of concentrates comprises an osmotic agent in substantially dry form.

186. (NEW) The apparatus of claim 185 wherein said osmotic agent comprises glucose.

187. (NEW) The apparatus of claim 184 wherein each of said respective plurality of concentrates comprises a single concentrate.

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188. (NEW) The apparatus of claim 184 wherein said corresponding plurality of concentrates comprises sodium chloride, sodium bicarbonate, magnesium chloride, calcium chloride, sodium lactate, lactic acid and glucose.

189. (NEW) The apparatus of claim 188 wherein said sodium chloride, sodium bicarbonate, magnesium chloride, calcium chloride, sodium lactate, lactic acid and glucose are in substantially dry form.

190. (NEW) The apparatus of claim 184 including a cleaning agent in one of said plurality of chambers.

191. (NEW) The apparatus of claim 184 including a controller for selectively controlling said mixer, whereby said apparatus can produce one of a plurality of different peritoneal dialysis solutions.

192. (NEW) The apparatus of claim 191 wherein said corresponding plurality of concentrates includes a corresponding plurality of electrolytes, wherein said controller can selectively produce one of a plurality of peritoneal dialysis solutions having different electrolyte concentrations.

193. (NEW) The apparatus of claim 191 wherein said controller includes input data means for receiving patient prescription information.

194. (NEW) The apparatus of claim 184 wherein said at least one of said corresponding plurality of concentrates is present in an amount such that when said one of said chambers containing said at least one of said corresponding plurality of concentrates is filled with a liquid, said at least one of said corresponding plurality of concentrates is only partially dissolved, and including a first flow line in fluid communication with said one of said chambers for removing said dissolved concentrate from said one of said chambers and a second flow line for substantially simultaneously adding a corresponding amount of liquid into said one of said chambers.

195. (NEW) The apparatus of claim 194 wherein said at least one of said corresponding plurality of concentrates is

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selected from the group consisting of sodium chloride and sodium bicarbonate.

196. (NEW) The apparatus of claim 194 wherein said at least one of said corresponding plurality of concentrates is present in an amount such that when said one of said chambers containing said at least one of said corresponding plurality of concentrates is filled with a liquid said at least one of said corresponding plurality of concentrates is substantially fully dissolved, and including priming means for priming said one of said chambers with water.

197. (NEW) The apparatus of claim 196 wherein said at least one of said corresponding plurality of concentrates is selected from the group consisting of magnesium chloride and calcium chloride.

198. (NEW) The apparatus of claim 184 wherein said at least one of said corresponding plurality of concentrates comprises first and second concentrates in substantially dry form, said first concentrate being disposed in a first one of said plurality of chambers and said second concentrate being disposed in a second one of said plurality of chambers, said first concentrate being present in said substantially dry form in said first one of said plurality of chambers in an amount such that when said first one of said plurality of chambers is filled with a liquid said first concentrate is only partially dissolved, said second concentrate being present in said second one of said plurality of chambers in said substantially dry form in an amount such that when said second one of said plurality of chambers is filled with a liquid said second concentrate is substantially fully dissolved, first priming means for priming said first concentrate with water, a first flow conduit for removing dissolved first concentrate from said first one of said plurality of chambers, a second flow conduit for substantially simultaneously adding a liquid in an amount corresponding to said liquid removed through said first flow conduit from said second one of said plurality of chambers, and second priming means for priming said second concentrate with water.

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199. (NEW) The apparatus of claim 184 wherein said one of said plurality of chambers comprises a first chamber, and said corresponding one of said plurality of concentrates in said first chamber comprises an osmotic agent, and including flow means for introducing water into said first chamber, for removing dissolved osmotic agent from said first chamber, and for reintroducing said dissolved osmotic agent into said first chamber.

200. (NEW) The apparatus of claim 199 including a heater for heating said dissolved osmotic agent circulating in said flow means.

201. (NEW) The apparatus of claim 199 including vent means for allowing the escape of gas from said dissolved osmotic agents circulating in said flow means.

202. (NEW) The apparatus of claim 199 wherein said osmotic agent comprises glucose.

203. (NEW) The apparatus of claim 184 wherein said sterilizer comprises a heat sterilizer for heating said peritoneal dialysis solution at an elevated pressure.

204. (NEW) The apparatus of claim 203 wherein said heat sterilizer is disposed downstream of said mixer.

205. (NEW) Apparatus for the preparation of a dialysis solution comprising a plurality of compartments including a first compartment, a corresponding plurality of chemical components for forming said dialysis solution including a first chemical component disposed in said first compartment comprising glucose in substantially dry form, a mixing module, and a plurality of flow paths for fluid communication of a liquid between said mixing module and said plurality of compartments to provide a plurality of chemical component solutions, including a first flow path for fluid communication between said mixing module and said first compartment to provide a glucose solution, said mixing module including a mixing chamber for mixing said glucose solution and said plurality of chemical component solutions so as to produce said dialysis solution.

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206. (NEW) The apparatus of claim 205 including a diffuser disposed in said first compartment to facilitate dissolution of said substantially dry glucose in said liquid.

207. (NEW) A method of peritoneal dialysis treatment with a dialysis solution produced at a predetermined patient location from a dialysis apparatus comprising a plurality of compartments including a first compartment and a corresponding plurality of components for said dialysis solution including a first component in substantially dry form, said method comprising combining a liquid and a first plurality of said plurality of components to provide a first plurality of component solutions, mixing said first plurality of component solutions to form said dialysis solution, flowing said dialysis solution into the peritoneal cavity of a patient, and draining said dialysis solution from said peritoneal cavity.

208. (NEW) The method of claim 207 wherein said first component comprises an osmotic agent.

209. (NEW) The method of claim 208 wherein said osmotic agent comprises glucose.

210. (NEW) The method of claim 207 including providing a flow of tap water for said dialysis apparatus, and purifying said flow of tap water to provide purified water, said liquid including said purified water.

211. (NEW) The method of claim 207 including sterilizing at least one of said liquid and said dialysis fluid in said dialysis apparatus.

212. (NEW) The method of claim 207 wherein said dialysis apparatus includes a processor and said plurality of compartments are disposed in a removable container, said method including connecting said removable container to said processor to initiate a treatment session and removing said removable container from said processor to terminate said treatment session.

213. (NEW) The method of claim 207 including sensing said concentrations of said first plurality of component solutions, providing said first plurality of component solutions

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to said mixing step, and regulating said providing of said first plurality of component solutions to said mixing step based on said sensing of said concentrations of said first plurality of component solutions.

214. (NEW) A method of providing an aqueous solution for medical use from a plurality of chambers including a first chamber and a corresponding plurality of concentrates disposed in said plurality of chambers including a first concentrate in substantially dry form in said first chamber, said method comprising priming said first concentrate with water to produce a first dissolved concentrate, flowing said first dissolved concentrate through a first flow regulator to provide a metered volume of said first concentrate, measuring the concentration of said metered volume of said first concentrate, whereby a first amount of said first concentrate is provided, and delivering said first amount of said first concentrate to a mixing vessel until said first amount comprises a predetermined amount of said first concentrate.

215. (NEW) The method of claim 214 including priming each of said plurality of concentrates with water to produce a plurality of dissolved concentrates, flow said plurality of dissolved concentrates through a plurality of flow regulators so as to provide a metered volume of each of said plurality of concentrates, measuring the concentration of each of said metered volumes of said plurality of concentrates whereby amounts of said plurality of concentrates are provided, and delivering said amounts of said concentrates to said mixing vessel until said amounts comprise predetermined amounts of said plurality of concentrates.

216. (NEW) The method of claim 214 wherein said delivering of said amounts of said plurality of concentrates to said mixing vessel comprises pumping said plurality of concentrates with a single pump.

217. (NEW) The method of claim 214 wherein said measuring of said concentrations of said metered volumes of said

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plurality of concentrates comprises using a single measuring means.

218. (NEW) The method of claim 214 including further diluting said first concentrate between said first chamber and said mixing vessel.

219. (NEW) The method of claim 218 wherein said further diluting of said first concentrate comprises pumping said first concentrate along a first flow line at a first metered rate, pumping water along a second flow line at a second metered rate, and mixing said first concentrate from said first flow line and said water from said second flow line to provide a diluted first concentrate.

220. (NEW) The method of claim 219 including measuring the concentration of at least one of said first concentrate and said diluted first concentrate and controlling said pumping of said first concentrate and said water so as to provide a predetermined concentration of said diluted concentrate.

221. (NEW) The method of claim 218 wherein said delivering of said first amount of said first concentrate to said mixing vessel comprises delivering said further diluted first concentrate to said mixing vessel at a first flow rate, and including measuring the concentration of said further diluted first concentrate, multiplying said measured concentration of said further diluted first concentrate with said first flow rate to provide a product, integrating said product over time to provide a total amount of said first concentrate delivered to said mixing vessel, and terminating said delivering of said further diluted first concentrate to said mixing vessel when said total amount of said first concentrate comprises a predetermined amount of said first concentrate.

222. (NEW) The method of claim 218 including measuring a predetermined property of said first concentrate or said further diluted first concentrate at a location downstream of said first chamber and comparing said measured property with an expected property of said first concentrate.

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223. (NEW) The method of claim 214 including passing said liquid from said mixing vessel for use with a patient and diluting said liquid at a point downstream of said mixing vessel to provide a diluted concentrate.

224. (NEW) The method of claim 223 including measuring the concentration of said diluted concentrate, and wherein said measuring of said concentration of said metered volume of said first concentrate and said measuring of said concentration of said diluted concentrate are carried out with the same measuring means.

225. (NEW) The method of claim 214 including flushing the path of said flowing of said first dissolved concentrate through said flow regulator.

226. (NEW) Apparatus for providing an aqueous solution for medical use from a plurality of concentrates including a first concentrate in substantially dry form comprising a plurality of chambers including a first chamber containing said first concentrate, priming means including a first conduit for supplying water to said first chamber to provide a first dissolved concentrate, a mixer for receiving said first dissolved concentrate, a flow regulator associated with said first dissolved concentrate for supplying said first dissolved concentrate to said mixer, measuring means for measuring the concentration of said first dissolved concentrate, and a first pump for pumping a metered volume of said first dissolved concentrate by means of said flow regulator to said mixer, whereby a predetermined amount of said first dissolved concentrate is delivered to said mixer.

227. (NEW) The apparatus of claim 226 wherein said flow regulator comprises a plurality of flow regulators associated with each of said plurality of concentrates for supplying each of said plurality of concentrates to said mixer, and said measuring means measures the concentration of each of said plurality of concentrates.

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228. (NEW) The apparatus of claim 226 wherein said pump is adapted to pump a metered volume of each of said plurality of concentrates to said mixer.

229. (NEW) The apparatus of claim 226 wherein said measuring means is adapted to measure the concentration of each of said plurality of concentrates.

230. (NEW) The apparatus of claim 226 including diluting means for diluting at least one of said plurality of concentrates to provide a diluted concentrate between one of said plurality of chambers associated with said at least one of said plurality of concentrates and said mixer.

231. (NEW) The apparatus of claim 230 including a concentrate conduit for carrying said metered volume of said first dissolved concentrate and a second pump for pumping a metered volume of water to said mixer, a water conduit for carrying said metered volume of water, said concentrate conduit and said water conduit being disposed whereby said water dilutes said first dissolved concentrate and provides a diluted concentrate prior to said mixer.

232. (NEW) The apparatus of claim 231 wherein said measuring means is adapted to measure the concentration of at least one of said first dissolved concentrate and said diluted concentrate, and a controller for controlling the rate of said first and second pumps whereby a diluted concentrate having a predetermined concentration is provided.

233. (NEW) The apparatus of claim 230 wherein said first pump passes said diluted concentrate to said mixing vessel at a first flow rate and said measuring means measures the concentration of said diluted concentrate, said apparatus including a processor for multiplying said measured concentration of said diluted concentrate by said first flow rate to provide a product, integrating said product over time, whereby the total amount of said concentrate delivered to said mixer is provided, and terminating said providing of said diluted concentrate to said mixer when said total amount of said concentrate delivered to said mixer reaches a predetermined amount.

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234. (NEW) The apparatus of claim 230 wherein said measuring means is adapted to measure a predetermined property of at least one of said first dissolved concentrate and said diluted concentrate, said apparatus including determining means for determining if said measured value of said predetermined property comprises a predetermined value of said predetermined property.

235. (NEW) The apparatus of claim 226 including diluting means disposed downstream of said mixer for providing a diluted concentrate, and a mixer conduit for withdrawing fluid from said mixer.

236. (NEW) The apparatus of claim 235 wherein said measuring means is adapted to also measure the concentration of said diluted concentrate.

237. (NEW) A method for the preparation of dialysis solution from a plurality of compartments and a corresponding plurality of chemical components in said plurality of compartments, said method comprising adding liquid to said plurality of compartments to form a plurality of dialysis solution constituents, combining a first plurality of said plurality of dialysis solution constituents excluding a portion of at least one of said plurality of dialysis solution constituents to provide said dialysis solution for use in a dialysis treatment session, and discarding said portion of said at least one of said plurality of dialysis solution constituents.

238. (NEW) A method for the preparation of a dialysis solution at a patient treatment location from a plurality of compartments and a corresponding plurality of chemical components disposed in said plurality of compartments, said method comprising adding a liquid to said plurality of compartments to provide a plurality of chemical component solutions, flowing said plurality of chemical component solutions to a mixer, monitoring said flow of at least one of said chemical component solutions to said mixer, and controlling said flow of said at least one of said chemical component solutions based on said monitoring thereof.

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239. (NEW) A method for the preparation of a dialysis solution at a patient treatment location comprising adding liquid to a plurality of chemical components including a first chemical component comprising glucose to form a plurality of chemical components solutions including a first chemical component solution comprising a glucose solution, mixing said plurality of chemical component solutions in a mixing module to form said dialysis solution, and connecting said mixing module into fluid communication with a patient dialysate line to permit said dialysis solution to flow from said mixing module to said patient dialysate line.

240. (NEW) A method for the preparation of a dialysis solution at a patient treatment location from a plurality of dialysis components including a first plurality of said plurality of dialysis components in substantially dry form, comprising priming said first plurality of said dialysis components to form a first plurality of dialysis component solutions, mixing at least a portion of said first plurality of dialysis components solutions to form a concentrate solution, and diluting said concentrate solution with liquid to form said dialysis solution.

241. (NEW) A method of performing a dialysis treatment using a plurality of chemical components to form a dialysis solution, said method comprising adding liquid to said plurality of chemical components to form a plurality of chemical component solutions, mixing at least a portion of said chemical component solutions in a mixing module to form a concentrated solution, diluting said concentrated solution in said mixing vessel with a liquid so as to form said dialysis solution, and dispensing said dialysis solution from said mixing module to a patient dialysate line.

242. (NEW) Apparatus for the selective formulation of a dialysis solution comprising a container including a plurality of compartments, a corresponding plurality of chemical components disposed in said plurality of compartments, whereby said plurality of chemical components can be combined with liquid to form a plurality of constituents of said dialysis solution, at

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least one module including a plurality of flow paths coupled to said plurality of compartments, whereby a source of liquid can be applied to said plurality of flow paths to provide said liquid to said plurality of compartments to form said plurality of constituents of said dialysis solution, a mixing chamber in fluid communication with said plurality of flow paths whereby said plurality of constituents can flow into said mixing chamber, at least one flow regulator for regulating said flow of said constituents from said plurality of compartments to said mixing chamber, and a controller for controlling said at least one flow regulator whereby the amounts of said constituents flowing to said mixing chamber can be adjusted.

243. (NEW) Apparatus for the preparation of peritoneal dialysis fluid at a treatment location, said apparatus comprising a plurality of chambers, a corresponding plurality of concentrates in each of said plurality of chambers, each of said plurality of concentrates comprising a constituent of said peritoneal dialysis fluid, a mixer for mixing said plurality of concentrates with a liquid to produce said peritoneal dialysis fluid, a controller for selectively controlling said mixer for producing one of a plurality of peritoneal dialysis fluids having different predetermined formulations, a sterilizer for sterilizing at least one of said liquid and said peritoneal dialysis fluid, and a patient connector in fluid communication with the peritoneal cavity of a patient for providing said peritoneal dialysis fluid to said patient, said controller including input data means for receiving said predetermined formulations whereby said mixer can be selectively controlled to produce said predetermined formulation of said peritoneal dialysis fluid.

244. (NEW) The apparatus of claim 243 wherein said corresponding plurality of concentrates comprises a corresponding plurality of electrolytes, whereby said controller can selectively produce said predetermined formulations having different relative electrolyte concentrations.

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245. (NEW) The apparatus of claim 243 wherein said plurality of chambers comprises a plurality of compartments in a single container, whereby all of said corresponding plurality of concentrates in said plurality of compartments are sufficient to provide said peritoneal dialysis fluid.

246. (NEW) Apparatus for the preparation of a peritoneal dialysis fluid at a treatment location comprising a plurality of chambers, a corresponding plurality of concentrates comprising constituents of said peritoneal dialysis fluid comprising a plurality of electrolytes, a mixer for mixing said plurality of concentrates with a liquid to produce said peritoneal dialysis fluid, a controller for selectively controlling said mixer to produce one of a plurality of predetermined peritoneal dialysis fluid formulations having a predetermined concentration of said electrolytes, a sterilizer for sterilizing at least one of said liquid and said peritoneal dialysis fluid, and a connector for fluid connection with a patient.

247. (NEW) The apparatus of claim 246 wherein said plurality of chambers are contained within a single container.

248. (NEW) The apparatus of claim 247 including a container engaging portion for engaging said container and urging said container into a predetermined position, whereby when said container in said predetermined position said plurality of chambers are in fluid communication with said apparatus.

249. (NEW) The apparatus of claim 248 wherein each of said plurality of chambers includes a chamber opening, and including a plurality of flanges adjacent to said plurality of chamber openings and a plurality of said container engaging portions, whereby said container engaging portions are adjusted to engage said plurality of flanges when in said predetermined position.

250. (NEW) The apparatus of claim 249 wherein said plurality of chamber openings are in linear alignment, and said container engaging portions comprise pairs of laterally spaced

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engaging members adapted to engage said plurality of flanges on opposite sides of said plurality of chamber openings.

251. (NEW) The apparatus of claim 246 including a plurality of penetrable seals associated with said plurality of chambers, and including a plurality of spikes adapted to penetrate said plurality of penetrable seals in order to open said plurality of chambers.

252. (NEW) The apparatus of claim 251 wherein each of said plurality of spikes comprises first and second fluid flow channels.

253. (NEW) The apparatus of claim 251 wherein said plurality of spikes comprise a pair of said spikes for penetrating said plurality of chambers, whereby at least three fluid flow channels can be provided thereby.

254. (NEW) The apparatus of claim 251 wherein said plurality of chambers are contained within a removable container, and including a plurality of covers for covering said plurality of spikes when said container is removed, whereby said spikes may be disinfected.

255. (NEW) The apparatus of claim 254 including container engaging portions for engaging said plurality of covers so as to urge said plurality of covers to cover said spikes.

256. (NEW) The apparatus of claim 243 including a water purifier comprising a first reverse osmosis membrane unit including an inlet, a purified water outlet, and a waste water outlet, and a second reverse osmosis membrane unit including an inlet, a purified water outlet, and a waste water outlet, said purified water outlet of said first reverse osmosis membrane unit being in fluid communication with said inlet of said second reverse osmosis membrane unit and said waste water outlet of said second reverse osmosis membrane unit being in fluid communication with said inlet of said first reverse osmosis membrane unit.

257. (NEW) The apparatus of claim 256 wherein said water purifier includes at least one coarse filter, a water softener, and a fine filter disposed upstream of said first reverse osmosis membrane unit.

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258. (NEW) The apparatus of claim 256 wherein said water purifier includes a degasser disposed upstream of said inlet of said first reverse osmosis membrane unit.

259. (NEW) Apparatus for the preparation of peritoneal dialysis fluid at a treatment location comprising a water inlet for receiving a supply of water from a water supply, a water purifier in fluid communication with said water inlet for purifying water from said water inlet, a mixer for mixing said purified water with dialysis fluid concentrate to produce a peritoneal dialysis fluid, a sterilizer in fluid communication with said mixer for sterilizing said peritoneal dialysis fluid, said sterilizer comprising a heat sterilizer for heat sterilizing said peritoneal dialysis fluid at a sterilizing temperature and elevated pressure, and a connector in fluid communication with said sterilizer for providing fluid communication for said sterilized peritoneal dialysis fluid with the peritoneal cavity of a patient.

260. (NEW) The apparatus of claim 259 wherein said heat sterilizer is disposed downstream of said mixer.

261. (NEW) The apparatus of claim 259 wherein said heat sterilizer includes a sterilization conduit whereby said heat sterilizer can sterilize said peritoneal dialysis fluid as it flows through said sterilization conduit.

262. (NEW) The apparatus of claim 261 including a fluid conduit disposed downstream of said heat sterilizer for fluid communication with said connector and a fluid cooler for cooling said sterilized peritoneal dialysis fluid flowing in said fluid conduit.

263. (NEW) The apparatus of claim 262 wherein said heat sterilizer is disposed along said fluid conduit upstream of said flow of sterilized peritoneal dialysis fluid to said connector.

264. (NEW) The apparatus of claim 259 wherein said heat sterilizer is adapted to heat said peritoneal dialysis fluid to a temperature of at least about 140°C.

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265. (NEW) The apparatus of claim 259 wherein said heat sterilizer is adapted to heat said peritoneal dialysis fluid so as to obtain an F_0 value of at least 20 minutes, wherein

$$F_0 = \int_0^L \frac{S}{Q} \times 10^{\left(\frac{T(y)-121}{10}\right)} dy$$

wherein:

- L comprises the length of a sterilization fluid flow path for said peritoneal dialysis fluid;
- S comprises the internal cross-sectional area of said sterilization fluid path;
- Q comprises the volumetric flow rate of said peritoneal dialysis fluid along said sterilization flow path; and
- T(y) comprises the temperature distribution of said peritoneal dialysis fluid as a function of the distance from the start of said sterilization flow path.

266. (NEW) A method of dialysis treatment of a patient with a dialysis treatment system including a connector and flow path, said method comprising connecting a patient dialysate conduit with said connector, flowing a dialysis solution along said flow path to said patient dialysate conduit, sterilizing said dialysis solution flowing to said patient dialysis conduit at a sterilization module in said dialysis treatment system, and sterilizing at least a substantial portion of said flow path including flowing a sterilization liquid in said flow path between said sterilization module and said connector.

267. (NEW) A dialysis system for providing a dialysis solution from tap water at a patient treatment location comprising a water treatment module for purifying said tap water, a mixing module connected to said water treatment module for mixing said purified tap water with a plurality of chemical components to provide said dialysis solution, and a connector connected to said mixing module and adapted to be connected to a patient dialysate conduit for flowing said dialysate solution thereto.

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comprising at least one input selected from the group consisting of reading information from a smart card, receiving information from a modem, and manually entering information on a user entry base.

273. (NEW) The method of claim 272 wherein said inputting of said information comprises inputting desired osmotic substance concentrations and wherein said forming of said predetermined formulation of said dialysis solution comprises formulating said formulation of said dialysis solution from said desired osmotic substance concentrations.

274. (NEW) The method of claim 271 wherein said forming of said predetermined formulation of said dialysis solution comprises adding a liquid to a plurality of chemical compositions, processing said predetermined prescription information in said processor, forming said predetermined formulation of said dialysis solution based on said predetermined prescription information in said processor, connecting said processor with said peritoneal cavity of said patient, flowing said predetermined formulation of said dialysis solution to said peritoneal cavity, removing said predetermined formulation of said dialysis solution from said peritoneal cavity, and disengaging said container from said processor.

275. (NEW) The method of claim 271 wherein said forming of said predetermined formulation of said dialysis solution comprises adding a liquid to a plurality of chemical compositions so as to form a plurality of chemical composition solutions, and mixing a plurality of predetermined quantities of said chemical composition solutions.

276. (NEW) The method of claim 275 wherein at least one of said chemical compositions is in substantially dry form.

277. (NEW) Dialysis apparatus comprising a water purification module including an inlet for tap water, at least one particulate filter in fluid communication with said inlet, a degasser for removing gas from said tap water, a first reverse osmosis membrane unit including a first inlet, a first purified water outlet, and a first waste water outlet, a second reverse

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osmosis membrane unit including a second inlet, a second purified water outlet, and a second waste water outlet, said first purified water outlet being in fluid communication with said second inlet and said second waste water outlet being in fluid communication with said first inlet, a thermal control and sterilization module in fluid communication with said water purification module and including a plurality of heat exchangers for conducting heat transfer between fluids flowing therein, a concentrate mixing module in fluid communication with said water purification module and said thermal control and sterilization module, said concentrate mixing module comprising a plurality of compartments, a corresponding plurality of concentrated components of said dialysis solution within said plurality of compartments, a plurality of fluid couplers including fluid channels including a first plurality of said fluid couplers adapted to be in fluid communication with predetermined one of said plurality of compartments, a plurality of valves for liquid flow regulation including a first plurality of said valves associated with a corresponding plurality of said plurality of fluid couplers whereby the flow of liquid to and from said plurality of compartments can be regulated thereby, a concentrate reservoir in fluid communication with said plurality of fluid couplers, at least one conductivity sensor for sensing the conductivity of a liquid flowing into said concentrate reservoir, a mixing chamber in fluid communication with said concentrate reservoir and with one of said first and second purified water outlets for forming said dialysis solution, at least one pump in fluid communication with said plurality of flow couplers, said concentrate reservoir and said mixing chamber, an outflow drain for discarding said liquid, and a connector for fluid communication with a patient dialysate line, said connector in fluid communication with said mixing chamber whereby said dialysis solution can flow to said patient dialysate line.

278. (NEW) The apparatus of claim 277 wherein said plurality of fluid couplers include a corresponding plurality of spikes adapted to extend into container ports.

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279. (NEW) The apparatus of claim 277 wherein said thermal control and sterilization module includes heating means for heating said dialysis fluid flowing from said mixing chamber to said connectors whereby said dialysis fluid can be sterilized.

REMARKS

The above-noted cancellation of claims 1-143, and addition of new claims 144-279, as well as the submission of a new Abstract and revisions to the Specification, are respectfully submitted prior to initiation of the prosecution of this application in the U.S. Patent and Trademark Office.

The above-noted new claims are respectfully submitted in order to more clearly and appropriately claim the subject matter which applicants consider to constitute their inventive contribution. No new matter is included in these amendments. In addition, the revisions to the Abstract and Specification are submitted in order to clarify and correct the Abstract and Specification and to conform them to all of the requirements of U.S. practice. No new matter is included in these amendments.

In view of the above, it is respectfully requested that these amendments now be entered, and that prosecution on the merits of this application now be initiated. If, however, for any reason the Examiner does not believe such action can be taken, it is respectfully requested that he telephone applicant's attorney at (908) 654-5000 in order to overcome any objections which he may have.

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If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge applicant's Deposit Account No. 12-1095 therefor.

Respectfully submitted,

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METHOD, APPARATUS AND COMPONENTS OF DIALYSIS SYSTEMS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application relies on the benefit of priority Swedish Patent application No. 9901165-2, filed March 30, 1999, the entire disclosure of which is incorporated herein by reference. In addition, related U.S. provisional patent application Serial No. 60/127,179, filed March 30, 1999, is also incorporated herein by reference.

~~Field of the Invention~~ FIELD OF THE INVENTION

[0002] The present invention relates to methods, apparatus and components of dialysis systems, such as peritoneal dialysis, hemodialysis, hemodiafiltration or hemofiltration systems.

~~Background of the Invention~~ BACKGROUND OF THE INVENTION

[0003] Kidney dysfunction is a serious and life-threatening condition wherein the kidneys of a mammal do not function properly to remove impurities, remove excess water and perform other physiologically important activities. A person affected with kidney dysfunction needs to undergo regular dialysis treatments so that the blood can be purified and water removed.

[0004] In one type of conventional dialysis procedure, peritoneal dialysis (PD), a PD fluid is administered to the peritoneal cavity of a mammalian patient to dwell there and later be removed as a spent dialysate. Waste products are transferred to the PD fluid and are removed together with the spent dialysate. An osmotic agent in the PD fluid causes removal of excess water. A buffer in the PD fluid causes replenishment of the body buffer. Further electrolytes are balanced by the PD fluid.

[0005] Because PD fluid is passed into the patient's body there is a risk of infection, which sometimes results in peritonitis.

[0006] For performing peritoneal dialysis, couplings are used for connecting a catheter ending in a peritoneal cavity to a source of PD fluid. In an attempt to reduce patient

infection, such couplings are made as "aseptic" or "sterile" couplings. Although aseptic couplings aid in reducing the contamination of PD fluid, each coupling may permit entry of potentially harmful microorganisms, such as bacteria and fungi, into an otherwise sterile PD system, and, eventually, being transfer to the peritoneal cavity. Reducing the number of these couplings may reduce the risk of infection and peritonitis.

[0007] Traditionally, sterile PD fluid is stored in, and administered to a patient from, a plastic fluid bag. An aseptic coupling is typically used to connect the fluid bags to the catheter of the patient. Each coupling increases the chances of bacterial and other contamination.

[0008] The two most common forms of PD, namely, continuous ambulatory peritoneal dialysis (CAPD) and automatic peritoneal dialysis (APD), require many fluid bags to be used per year. CAPD normally relies on gravity to fill and drain PD fluid originating in a bag set and provides continuous treatment while the patient is still relatively free to move. Fluid exchanges are normally performed during the daytime. APD relies on the use of a cyclor for pumping PD fluid from fluid bags to perform patient fill and drain cycles, usually overnight, while the patient is asleep. In both cases, a particular prescription of PD fluid is manufactured and ~~packeaged~~ packaged in one or more bags under sterile conditions at a production plant, and the bags are then shipped to a patient or physician.

[0009] However, the use of PD fluid bags has a number of drawbacks and disadvantages. Every patient has different dialysis requirements, and those requirements may be different at different times, and therefore benefits from use of a PD fluid that specifically meets the patient's needs. As a result, manufacturers of PD fluid have to make and deliver many different formulations of PD fluid. This often requires storage of a significant number of bags containing different PD fluid formulations in the home of a patient.

[0010] Clinical testing is being performed today using bicarbonate as a buffer instead of conventional lactate buffered PD fluid. Conventional PD fluids have a relatively low pH, which may cause discomfort and even pain during the fill phase. By using bicarbonate as a buffer, PD fluids having a physiological pH may be formulated. However, over time, calcium carbonate, formed from components of the PD fluid, may precipitate out of the solution of the PD fluid, rendering the solution unusable.

[0011] Glucose, another component of PD fluid, may degrade over time particularly when the PD fluid has been subject to conventional heat ~~sterilisation~~ sterilization in an autoclave. The degradation of glucose may produce degradation products which are potentially harmful to the patient, at least in the long term.

[0012] PD fluid bags are often shipped a significant distance from the point of manufacture to the point of use. Since a large proportion of PD fluid is water, this effectively amounts to transporting large quantities of water from PD fluid production plants to treatment locations, such as hospitals, clinics or patients' homes.

[0013] Further, the size of PD fluid bags is limited because they ~~muust~~ must be sufficiently lightweight to permit easy handling by a patient or physician. Most PD fluid bags for CAPD contain a relatively small amount of fluid, for example between 0.5 and 5-~~litres~~ liters. When higher volumes are required, such as in APD, multiple PD fluid bags may be used during each treatment session. Having more than one PD fluid bag, however, necessitates an aseptic coupling for each bag and requires relatively complicated connection and disconnection procedures when changing bags. These additional connection and disconnection procedures, although aseptic, provide an opportunity for potentially harmful bacteria to enter the dialysis system and cause peritonitis. Four or five connections may be involved in APD.

[0014] In dialysis, specifically acute hemodialysis, bags

of sterile dialysis solution are used. During hemofiltration and hemodiafiltration, infusion solutions are used for infusion into the blood. Such solutions have the same problems as outlined above.

[0015] In U.S. Patent No. 4,718,890, U.S. Patent No. 4,747,822, U.S. Patent No. 5,004,459 and U.S. Patent No. 5,643,201, it has been proposed to make up and administer PD fluid at a treatment location. However, these proposed approaches have various drawbacks and disadvantages. U.S. Patent No. 5,643,201 is illustrative. It discloses a system for preparation of PD fluid, using a concentrated dialysis liquid source as a starting point. In the system, water is purified in a reverse osmosis unit and is then mixed by a volumetric proportioning pump with the liquid concentrate. Additional dextrose solution may be added by a dextrose pump. The mixed fluid is heated to a temperature of 70°C to 80°C and is then cooled to a proper patient temperature, passed to a reservoir where it is weighed to check the amount, and then delivered to the peritoneal cavity of the patient. Since this system uses a concentrated solution as the PD fluid concentrate, there may be problems due to the stability of the concentrates, for example if bicarbonate buffer is used. In addition, the proposed temperature of 70°C to 80°C may not be adequate to achieve a sufficiently high level of sterilisationsterilization.

[0016] Further, although there is an option of adding additional dextrose, the relative concentrations of the electrolyte components of the PD fluid are fixed by their relative concentrations in their initially concentrated form. Thus, the basic formulation of the PD fluid, apart from the dextrose concentration, is predetermined in advance by the proportions of the constituent substances in the initial concentrated dialysis liquid source. If the system were to be useable with different prescriptions, it would be necessary to provide a range of different concentrated dialysis liquid sources each having the constituent substances present in the

appropriate proportions for that prescription. Thus, a range of sources, such as bags of concentrated dialysis liquid, would be required, leading essentially to the same logistic problem as in the PD treatment systems where the PD fluid is entirely pre-prepared at a remote point of manufacture.

[0017] Another proposal for making aqueous solutions for medical purposes, including PD fluid, is disclosed in GB British Patent No. 1,450,030. This also uses a concentrated solution as a starting point. Relative concentrations of electrolyte are predetermined by the starting concentrated solution. This proposal from 1972 does not provide detail on how the PD fluid would be delivered to a patient.

[0018] In light of the foregoing, there is a need in the art for improving peritoneal dialysis techniques.

SUMMARY OF THE INVENTION

[0019] In accordance with the present invention, these and other objects have now been realized by the invention of a container for use in the preparation of a peritoneal dialysis fluid, the container comprising a plurality of chambers, and a corresponding plurality of concentrates for the peritoneal dialysis fluid, at least one of the plurality of concentrates in at least one of the chambers comprising a concentrate in the form of a powder.

[0020] In accordance with one embodiment of the present invention, a container is provided for use in the preparation of a dialysis fluid, the container comprises a plurality of chambers, a cleaning agent disposed in at least one of the plurality of chambers, and a powdered inorganic salt disposed in at least one other of the plurality of chambers.

[0021] In accordance with another embodiment of the present invention, a container is provided for use in the preparation of a dialysis fluid, the container comprising a plurality of chambers, a first amount of a first inorganic salt disposed in at least one of the plurality of chambers, and a second amount of a second inorganic salt different from the first inorganic salt disposed in another of the plurality of chambers, the at

least one of the plurality of chambers having a first volume and the another of the plurality of chambers having a second volume, whereby when the first and second inorganic salts are prepared by filling the at least one and the another of the plurality of chambers with a liquid to provide solutions of first and second inorganic salts, the solutions of the first and second inorganic salts have characteristically different conductivities.

[0022] In accordance with another embodiment of the present invention, a container is provided for use in the preparation of a dialysis fluid, the container comprising a plurality of distinct chambers, a corresponding plurality of concentrate components of the dialysis fluid in the plurality of distinct chambers, and a corresponding plurality of connectors for each of the plurality of distinct chambers, each of the plurality of connectors including at least two separate fluid channels so as to provide for simultaneous inflow and outflow from each of the plurality of distinct chambers.

[0023] In accordance with yet another embodiment of the container of the present invention, the container is used for priming powdered glucose at a predetermined patient location, the container including an upper region and a lower region, the powdered glucose, an inlet port in the lower region for receiving a supply of water to dissolve the powdered glucose, and a diffuser associated with the inlet port for diffusing the flow of water into the powdered glucose.

[0024] In accordance with another embodiment of the container of the present invention, the container is used in connection with a dialysis fluid, the container comprising a plurality of distinct chambers, and a corresponding plurality of connectors for each of the plurality of distinct chambers, each of the plurality of connectors being aligned along a predetermined linear axis.

[0025] In accordance with another embodiment of the container of the present invention, the container comprises a universal container for use in connection with a dialysis

solution, the universal container including a plurality of compartments, a corresponding plurality of predetermined amounts of chemical components in each of the plurality of compartments, wherein upon combination with a liquid the plurality of chemical components can provide a plurality of different formulations of the dialysis solution for a corresponding plurality of patient requirements, and at least one port associated with the plurality of compartments for providing fluid communication with a dialysis treatment system.

[0026] In accordance with another embodiment of the container of the present invention, a container is provided for use in the preparation of a dialysis fluid, the container including a first compartment, calcium chloride in the first compartment, a second compartment, magnesium chloride in the second compartment, a third compartment, sodium chloride in the third compartment, a fourth compartment, a cleaning agent in the fourth compartment, a fifth compartment, sodium bicarbonate in the fifth compartment, a sixth compartment, glucose in the sixth compartment, a plurality of ports associated with each of the first, second, third, fourth, fifth and sixth compartments whereby the plurality of ports can be connected to a dialysis treatment unit for preparation of the dialysis solution at a patient treatment location.

[0027] In accordance with another embodiment of the container of the present invention, a container is provided for use in connection with dialysis comprising a plurality of compartments including a first compartment, an ionic component of a dialysis solution disposed in the first compartment, a second compartment, and a cleaning agent or a precursor of the cleaning agent for cleaning a flow path in a dialysis system disposed in the second compartment, the container including a plurality of ports whereby the first and second compartments can be placed in fluid communication with the dialysis system.

[0028] In accordance with another embodiment of the container of the present invention, the container includes a

surface having a longitudinal axis for use in connection with dialysis comprising a plurality of compartments, a corresponding plurality of chemical compositions in each of the plurality of compartments, and a plurality of fluid ports in fluid communication with each of the plurality of compartments, whereby each of the plurality of compartments can be placed in fluid communication with a dialysis system, at least one of the plurality of ports being disposed along the surface of the container asymmetrically with respect to the longitudinal axis of the surface of the container.

[0029] In accordance with another embodiment of the container of the present invention, a container is provided for use in connection with dialysis including a plurality of compartments, a corresponding plurality of chemical components in each of the plurality of compartments, a plurality of ports associated with each of the plurality of compartments for fluid communication with a dialysis system, and readable indicia disposed on the container, the readable indicia being indicative of the contents of the plurality of compartments, whereby the readable indicia can be recognized by the dialysis system.

[0030] In accordance with another embodiment of the container of the present invention, a container is provided for use in connection with dialysis comprising a first compartment including a first air vent channel, a first fluid channel and a first port in fluid communication with the first air vent channel and the first fluid channel, a second compartment including a second air vent channel, a second fluid channel, and a second port in fluid communication with the second air vent channel and the second fluid channel, a third compartment including a third air vent channel, a third fluid channel, and a third port in fluid communication with the third air vent channel and the third fluid channel, a fourth compartment including a fourth air vent channel, a first fourth port in fluid communication with the fourth air vent channel, a fluid input channel, and a diffuser in fluid

communication with the fluid input channel, a fluid output channel, a second fourth port in fluid communication with the fluid input channel and the fluid output channel, and a glucose filter in fluid communication with the fluid output channel, a fifth compartment including a fifth air vent channel, a fifth fluid channel, and a fifth port in fluid communication with the fifth air vent channel and the fifth fluid channel, a sixth compartment including a first air vent/fluid flow channel, a first fluid input/output channel and a sixth port in fluid communication with the first air vent/fluid flow channel and the first fluid input/output channel, a seventh compartment including a second air vent/fluid flow channel, a second fluid input/output channel, and a seventh port in fluid communication with the second air vent/fluid flow channel and the second fluid input/output channel, the plurality of compartments being sized to contain respective amounts of the components of the dialysis solution, the ports being placeable in fluid communication with a dialysis processing machine.

[0031] In accordance with the present invention, apparatus is also provided for the production of peritoneal dialysis solution comprising a plurality of chambers, a corresponding plurality of concentrates of constituents of the peritoneal dialysis solution, a mixer for mixing the corresponding plurality of concentrates with a predetermined liquid to produce the peritoneal dialysis solution, a sterilizer for sterilizing at least one of the peritoneal dialysis solution and the predetermined liquid, and a patient connector for supplying the peritoneal dialysis solution to the peritoneal cavity of the patient, at least one of the corresponding plurality of concentrates comprising a concentrate in substantially dry form, whereby in use the concentrate in the substantially dry form can be at least partially dissolved to be included in the peritoneal dialysis solution.

[0032] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for

the preparation of a dialysis solution comprising a plurality of compartments including a first compartment, a corresponding plurality of chemical components for forming the dialysis solution including a first chemical component disposed in the first compartment comprising glucose in substantially dry form, a mixing module, and a plurality of flow paths for fluid communication of a liquid between the mixing module and the plurality of compartments to provide a plurality of chemical component solutions, including a first flow path for fluid communication between the mixing module and the first compartment to provide a glucose solution, the mixing module including a mixing chamber for mixing the glucose solution and the plurality of chemical component solutions so as to produce the dialysis solution.

[0033] In accordance with the present invention, a method is also provided for peritoneal dialysis treatment with a dialysis solution produced at a predetermined patient location from a dialysis apparatus comprising a plurality of compartments including a first compartment and a corresponding plurality of components for the dialysis solution including a first component in substantially dry form, the method comprising combining a liquid and a first plurality of the plurality of components to provide a first plurality of component solutions, mixing the first plurality of component solutions to form the dialysis solution, flowing the dialysis solution into the peritoneal cavity of a patient, and draining the dialysis solution from the peritoneal cavity.

[0034] In accordance with another embodiment of the method of the present invention, the method includes providing an aqueous solution for medical use from a plurality of chambers including a first chamber and a corresponding plurality of concentrates disposed in the plurality of chambers including a first concentrate in substantially dry form in the first chamber, the method comprising priming the first concentrate with water to produce a first dissolved concentrate, flowing the first dissolved concentrate through a first flow regulator

to provide a metered volume of the first concentrate, measuring the concentration of the metered volume of the first concentrate, whereby a first amount of the first concentrate is provided, and delivering the first amount of the first concentrate to a mixing vessel until the first amount comprises a predetermined amount of the first concentrate.

[0035] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for an aqueous solution for medical use from a plurality of concentrates including a first concentrate in substantially dry form comprising a plurality of chambers, including a first chamber containing the first concentrate, priming means including a first conduit for supplying water to the first chamber to provide a first dissolved concentrate, a mixer for receiving the first dissolved concentrate, a flow regulator associated with the first dissolved concentrate for supplying the first dissolved concentrate to the mixer, measuring means for measuring the concentration of the first dissolved concentrate, and a first pump for pumping a metered volume of the first dissolved concentrate by means of the flow regulator to the mixer, whereby a predetermined amount of the first dissolved concentrate is delivered to the mixer.

[0036] In accordance with another embodiment of the method of the present invention, a method is provided for the preparation of dialysis solution from a plurality of compartments and a corresponding plurality of chemical components in the plurality of compartments, the method comprising adding liquid to the plurality of compartments to form a plurality of dialysis solution constituents, combining a first plurality of the plurality of dialysis solution constituents excluding a portion of at least one of the plurality of dialysis solution constituents to provide the dialysis solution for use in a dialysis treatment session, and discarding the portion of the at least one of the plurality of dialysis solution constituents.

[0037] In accordance with another embodiment of the method

of the present invention, a method is provided for the preparation of a dialysis solution at a patient treatment location from a plurality of compartments and a corresponding plurality of chemical components disposed in the plurality of compartments, the method comprising adding a liquid to the plurality of compartments to provide a plurality of chemical component solutions, flowing the plurality of chemical component solutions to a mixer, monitoring the flow of at least one of the chemical component solutions to the mixer, and controlling the flow of at least one of the chemical component solutions based on the monitoring thereof.

[0038] In accordance with another embodiment of the method of the present invention, a method is provided for the preparation of a dialysis solution at a patient treatment location comprising adding liquid to a plurality of chemical components including a first chemical component comprising glucose to form a plurality of chemical components solutions including a first chemical component solution comprising a glucose solution, mixing the plurality of chemical component solutions in a mixing module to form the dialysis solution, and connecting the mixing module into fluid communication with a patient dialysate line to permit the dialysis solution to flow from the mixing module to the patient dialysate line.

[0039] In accordance with another embodiment of the method of the present invention, a method is provided for the preparation of a dialysis solution at a patient treatment location from a plurality of dialysis components including a first plurality of the plurality of dialysis components in substantially dry form, comprising priming the first plurality of the dialysis components to form a first plurality of dialysis component solutions, mixing at least a portion of the first plurality of dialysis components solutions to form a concentrate solution, and diluting the concentrate solution with liquid to form the dialysis solution.

[0040] In accordance with another embodiment of the method of the present invention, a method is provided for performing

a dialysis treatment using a plurality of chemical components to form a dialysis solution, the method comprising adding liquid to the plurality of chemical components to form a plurality of chemical component solutions, mixing at least a portion of the chemical component solutions in a mixing module to form a concentrated solution, diluting the concentrated solution in the mixing vessel with a liquid so as to form the dialysis solution, and dispensing the dialysis solution from the mixing module to a patient dialysate line.

[0041] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for the selective formulation of a dialysis solution comprising a container including a plurality of compartments, a corresponding plurality of chemical components disposed in the plurality of compartments, whereby the plurality of chemical components can be combined with liquid to form a plurality of constituents of the dialysis solution, at least one module including a plurality of flow paths coupled to the plurality of compartments, whereby a source of liquid can be applied to the plurality of flow paths to provide the liquid to the plurality of compartments to form the plurality of constituents of the dialysis solution, a mixing chamber in fluid communication with the plurality of flow paths whereby the plurality of constituents can flow into the mixing chamber, at least one flow regulator for regulating the flow of the constituents from the plurality of compartments to the mixing chamber, and a controller for controlling the at least one flow regulator whereby the amounts of the constituents flowing to the mixing chamber can be adjusted.

[0042] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for the preparation of peritoneal dialysis fluid at a treatment location, the apparatus comprising a plurality of chambers, a corresponding plurality of concentrates in each of the plurality of chambers, each of the plurality of concentrates comprising a constituent of the peritoneal dialysis fluid, a

mixer for mixing the plurality of concentrates with a liquid to produce the peritoneal dialysis fluid, a controller for selectively controlling the mixer for producing one of a plurality of peritoneal dialysis fluids having different predetermined formulations, a sterilizer for sterilizing at least one of the liquid and the peritoneal dialysis fluid, and a patient connector in fluid communication with the peritoneal cavity of a patient for providing the peritoneal dialysis fluid to the patient, the controller including input data means for receiving the predetermined formulations whereby the mixer can be selectively controlled to produce the predetermined formulation of the peritoneal dialysis fluid.

[0043] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for the preparation of a peritoneal dialysis fluid at a treatment location comprising a plurality of chambers, a corresponding plurality of concentrates comprising constituents of the peritoneal dialysis fluid comprising a plurality of electrolytes, a mixer for mixing the plurality of concentrates with a liquid to produce the peritoneal dialysis fluid, a controller for selectively controlling the mixer to produce one of a plurality of predetermined peritoneal dialysis fluid formulations having a predetermined concentration of the electrolytes, a sterilizer for sterilizing at least one of the liquid and the peritoneal dialysis fluid, and a connector for fluid connection with a patient.

[0044] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for the preparation of peritoneal dialysis fluid at a treatment location comprising a water inlet for receiving a supply of water from a water supply, a water purifier in fluid communication with the water inlet for purifying water from the water inlet, a mixer for mixing the purified water with dialysis fluid concentrate to produce a peritoneal dialysis fluid, a sterilizer in fluid communication with the mixer for sterilizing the peritoneal dialysis fluid, the sterilizer

comprising a heat sterilizer for heat sterilizing the peritoneal dialysis fluid at a sterilizing temperature and elevated pressure, and a connector in fluid communication with the sterilizer for providing fluid communication for the sterilized peritoneal dialysis fluid with the peritoneal cavity of a patient.

[0045] In accordance with another embodiment of the method of the present invention, a method is provided for dialysis treatment of a patient with a dialysis treatment system including a connector and flow path, the method comprising connecting a patient dialysate conduit with the connector, flowing a dialysis solution along the flow path to the patient dialysate conduit, sterilizing the dialysis solution flowing to the patient dialysis conduit at a sterilization module in the dialysis treatment system, and sterilizing at least a substantial portion of the flow path including flowing a sterilization liquid in the flow path between the sterilization module and the connector.

[0046] In accordance with the present invention, a dialysis system is also provided for providing a dialysis solution from tap water at a patient treatment location comprising a water treatment module for purifying the tap water, a mixing module connected to the water treatment module for mixing the purified tap water with a plurality of chemical components to provide the dialysis solution, and a connector connected to the mixing module and adapted to be connected to a patient dialysate conduit for flowing the dialysate solution thereto.

[0047] In accordance with another embodiment of the apparatus of the present invention, an apparatus is provided for providing a predetermined dialysis solution from a plurality of dialysis components utilizing predetermined prescription information comprising a processor for processing the predetermined prescription information, a mixing module for mixing the plurality of dialysis components to form the dialysis solution, a controller for controlling the mixing module based on the predetermined prescription information

whereby the mixing module can form the dialysis solution with predetermined required amounts of each of the plurality of dialysis components.

[0048] In accordance with another embodiment of the method of the present invention, a method has been provided for peritoneal dialysis using a dialysis solution prepared at a patient treatment location based on predetermined prescription information, the method comprising providing a processor disposed at the patient treatment location for forming the dialysis solution from a plurality of dialysis components, providing the processor with a container including a predetermined quantity of each of the plurality of dialysis components whereby a plurality of different formulations of the dialysis solutions can be prepared therefrom, processing information regarding the predetermined prescription information in the processor, forming a predetermined formulation of the dialysis solution in the processor based on the predetermined prescription information, connecting the processor to the peritoneal cavity of the patient, flowing the predetermined formulation of the dialysis solution into the peritoneal cavity, removing the predetermined formulation of the dialysis solution from the peritoneal cavity, and disengaging the container from the processor.

[0049] In accordance with the present invention, dialysis apparatus is also provided comprising a water purification module including an inlet for tap water, at least one particulate filter in fluid communication with the inlet, a degasser for removing gas from the tap water, a first reverse osmosis membrane unit including a first inlet, a first purified water outlet, and a first waste water outlet, a second reverse osmosis membrane unit including a second inlet, a second purified water outlet, and a second waste water outlet, the first purified water outlet being in fluid communication with the second inlet and the second waste water outlet being in fluid communication with the first inlet, a thermal control and sterilization module in fluid

communication with the water purification module and including a plurality of heat exchangers for conducting heat transfer between fluids flowing therein, a concentrate mixing module in fluid communication with the water purification module and the thermal control and sterilization module, the concentrate mixing module comprising a plurality of compartments, a corresponding plurality of concentrated components of the dialysis solution within the plurality of compartments, a plurality of fluid couplers including fluid channels including a first plurality of the fluid couplers adapted to be in fluid communication with predetermined one of the plurality of compartments, a plurality of valves for liquid flow regulation including a first plurality of the valves associated with a corresponding plurality of the plurality of fluid couplers whereby the flow of liquid to and from the plurality of compartments can be regulated thereby, a concentrate reservoir in fluid communication with the plurality of fluid couplers, at least one conductivity sensor for sensing the conductivity of a liquid flowing into the concentrate reservoir, a mixing chamber in fluid communication with the concentrate reservoir and with one of the first and second purified water outlets for forming the dialysis solution, at least one pump in fluid communication with the plurality of flow couplers, the concentrate reservoir and the mixing chamber, an outflow drain for discarding the liquid, and a connector for fluid communication with a patient dialysate line, the connector in fluid communication with the mixing chamber whereby the dialysis solution can flow to the patient dialysate line.

[0050] Accordingly, the present invention is directed to apparatus and methodology that substantially obviate one or more of the short-comings or disadvantages of the related relevant art.

[0051] One object of the present invention is to prepare a medical fluid at a patient treatment site by mixing substantially water with one or more concentrates. The fluid may be prepared with ordinary tap water. As a result, a

patient's treatment requirements can be met through a compact package of concentrates, as opposed to multiple bags of fluid. This is convenient both for the patient and for the patient's doctor. It also reduces weight and volume and, accordingly, storage and transportation costs, as well as improving the logistics. Fewer disposable components may be used, involving the use of less plastic, and giving significant environmental advantages.

[0052] Another object of the present invention is to provide one or more components of medical fluid in at least substantially dry form to increase shelf life and/or problems associated with component precipitation. At least glucose may be provided in substantially dry form.

[0053] An additional object of the present invention is to provide a universal or near-universal (referred to as "universal" herein) container for filling multiple patient prescriptions. The administering machine is controlled to mix the appropriate prescription at the treatment site. As a result, multiple prescriptions can be obtained using a universal container or cartridge. This reduces the need to inventory multiple prescriptions.

[0054] Still another object of the present invention is to provide a container containing at least one concentrate in combination with a cleaning agent. In this way, the treatment and cleaning agents are conveniently packaged together.

[0055] Yet another object of the present invention is to provide a medical treatment apparatus having a reduced number of aseptic connections. There may be zero or only one aseptic connection. This reduces the risk of infections such as peritonitis.

[0056] A further object of the present invention is to provide a system whereby a patient's prescription can be electronically communicated to the dialysis machine, such as through a smart card. In this way, if a patient's prescription changes, the machine can be reprogrammed, while continuing to use the same universal cartridge.

[0057] A yet further object of the present invention is to provide a system offering higher fluid doses in peritoneal dialysis treatment without significant additional cost, unlike in conventional peritoneal dialysis systems in which the cost is roughly proportional to the fluid volume. Higher fluid volumes also may mean that a patient, who would normally be switched from conventional PD to another mode of treatment, such as hemodialysis (HD) because conventional PD provides inadequate treatment, may be kept on PD for a longer time.

[0058] A still further object of the present invention is to provide a system for ~~sterilising~~sterilizing peritoneal dialysis fluid immediately before delivery to a patient in order to minimise the chance of viable bacteria entering the peritoneum.

[0059] It should be understood that the present invention could still be practised without performing one or more of the objects and/or advantages set forth above, or by imperfectly performing certain of the objects and/or advantages. Still other objects and advantages will become apparent from the following description of the invention and the claims.

[0060] To achieve these and other objects and advantages, and in accordance with the purpose of the present invention, as embodied and broadly described herein, the invention includes a number of ~~aspects~~ embodiments.

[0061] Viewed from a first aspect, the present invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising: a plurality of chambers, each containing a respective concentrate of a constituent of the peritoneal dialysis fluid; a fluid mixer arranged to mix the concentrates with liquid to produce peritoneal dialysis fluid; a ~~steriliser~~sterilizer arranged to ~~sterilise~~sterilize at least one of the liquid and the peritoneal dialysis fluid; and a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal cavity of a

patient, and furthermore wherein
~~characterised in that~~

at least one of the concentrates is in substantially dry form and, in use of the apparatus, it is at least partially dissolved to form part of the peritoneal dialysis fluid.

[0062] The present invention also provides a method of producing peritoneal dialysis fluid at a treatment location and introducing the fluid into the peritoneal cavity of a patient, the method comprising:

providing a plurality of concentrates of constituents of the peritoneal dialysis fluid in respective chambers;

mixing the concentrates with liquid to obtain peritoneal dialysis fluid;

~~sterilising~~ sterilizing at least one of the liquid and the peritoneal dialysis fluid; and

introducing the peritoneal dialysis fluid to the peritoneal cavity of a patient; and furthermore wherein

~~characterised in that~~

at least one of the concentrates is in substantially dry form and is at least partially dissolved to form part of the peritoneal dialysis fluid.

[0063] By providing a concentrate in substantially dry or solid form, for example as a powder, the problems associated with liquid concentrates, such as precipitation, short shelf-life etc., can be minimised.

[0064] At least one of the concentrates is an osmotic agent, such as a carbohydrate, gluconate, peptides, ketoacid, glycerol, glucose polymer, disaccharide, etc. In one embodiment, the osmotic agent is glucose or dextrose. When glucose is provided as a solution, it generally has a limited shelf-life before it has to be used. By providing the osmotic agent in substantially dry or solid form and then dissolving it at the point of use, its shelf-life may be increased.

[0065] At least one of the concentrates is a buffer, such as bicarbonate, lactate, acetate, pyruvate, hydroxybutyrate, phosphate, etc. In one embodiment, sodium bicarbonate or

sodium ~~laeate~~-lactate or a combination thereof, is used as a buffer. By providing sodium bicarbonate in substantially dry or solid form, problems with solutions degrading by the precipitation of solids can be avoided. Sodium bicarbonate is sometimes ~~faveured~~-favored as a buffer for physiological reasons, but often another buffer is used in peritoneal dialysis. Thus, the use of substantially dry sodium bicarbonate, which is then freshly dissolved into solution at a treatment location, in a peritoneal dialysis treatment system, is beneficial.

[0066] A concentrate provided in a particular chamber may comprise more than one substance, for example some or all of the electrolytes may be provided in one chamber, and an osmotic agent may be provided in another chamber. In one embodiment, each concentrate comprises a separate constituent substance of the peritoneal dialysis fluid. For the production of a peritoneal dialysis fluid, each chamber may contain a separate constituent substance of the peritoneal dialysis fluid, selected from a group comprising: sodium chloride, sodium bicarbonate, magnesium chloride, calcium chloride, sodium lactate, lactic acid and glucose.

[0067] One or more of the concentrates may be provided in liquid form, and one or more of the concentrates may be provided in substantially dry form. In one embodiment the concentrates comprise: sodium chloride in substantially dry form; sodium bicarbonate in substantially dry form; magnesium chloride in substantially dry form; calcium chloride in substantially dry form; lactic acid solution; and glucose in substantially dry form.

[0068] By providing a plurality of concentrates of the constituents of peritoneal dialysis fluid in respective chambers, in accordance with the first aspect of the present invention, it becomes possible to produce peritoneal dialysis fluids of different formulations. The apparatus comprises a controller for controlling the fluid mixer to produce such different formulations. There is thus provided a choice of

formulations which can be made using the plurality of concentrates and liquid, such as purified water. For example, a single disposable container containing the concentrates can be used to produce different formulations as required by a prescription of a patient. This is considerably more convenient than the currently available systems for providing peritoneal dialysis fluids to a patient, in which the manufacturer stocks a range of bags of fluids of different formulations and the user has to be supplied with and choose the right bag for his or her treatment. Instead, the user can always be supplied with the same plurality of concentrates, which can then be used by the apparatus to make the required formulation.

[0069] In one embodiment, the concentrates comprise a plurality of electrolytes and the controller is operable to produce peritoneal dialysis fluid formulations having different relative concentrations of electrolytes. Thus, rather than being able merely to vary the concentration of osmotic agent (e.g. glucose), the apparatus can vary the relative concentrations of the electrolytes in the peritoneal dialysis fluid according to a patient's prescription. This is an advance over the previously proposed systems for producing peritoneal dialysis fluid at a treatment location using a single combined source of electrolytes. The electrolytes used in the peritoneal dialysis fluid may be one or more of sodium bicarbonate, sodium chloride, sodium lactate, magnesium chloride and calcium chloride.

[0070] The controller is in one embodiment provided with data input means for receiving prescription information for a patient. Such data input means may comprise a keyboard or touch screen or the like for a person to input the required prescription information. In one embodiment, the data input means comprises a memory device, for example a smart card, which may be inserted in a suitable part of the apparatus. Alternatively, or additionally, the data input means may comprise a modem or other means enabling remote communication,

for example for supervision or for transmission of prescription information to the apparatus.

[0071] It is possible to effect dissolution of substantially dry or solid concentrates in the chamber in which it is supplied. In the case of some concentrates, a relatively large quantity of solution may be needed, such that the chamber will generally not be large enough, without becoming cumbersome, to receive enough water to dissolve all the concentrate. Examples of such concentrates in a peritoneal dialysis solution are sodium chloride and sodium bicarbonate. In these cases, more than a single chamber volume of water is used to dissolve the concentrate. One way of doing this would be to fill the chamber with water via-through an opening, to then ~~to~~ empty the chamber by a reversed flow through the same opening, using an air vent to allow air ~~in~~ to fill the chamber during emptying (if the chamber walls are relatively rigid, an air vent not being necessary in the case of a flexible walled chamber). Filling would then take place again, and the process would be repeated as many times as necessary.

[0072] In another ~~arrangement~~ embodiment, the apparatus is arranged to prime ~~said~~the at least one concentrate in substantially dry form in a respective chamber with liquid comprising water, the amount of concentrate in the chamber and the size of the chamber being such that the concentrate is only partially dissolved when the chamber is filled with liquid, the apparatus further comprising a flow line for removing liquid comprising dissolved concentrate from the chamber, and a flow line for substantially simultaneously adding the same amount of liquid as removed to ~~said~~the chamber.

[0073] With such an arrangement, after initial priming a continuous flow to the fluid mixer can be obtained, rather than a periodic flow, reducing the number of cycles required, and thus the opportunities for inaccuracies, for a given batch of peritoneal dialysis ~~fluid~~ fluid. Thus, two flow lines are provided for simultaneous use. One of these may conveniently

be used for priming, and the other for venting air from the container, an air vent being necessary in the case of a rigid walled chamber. The concentrate removal flow line may be used during priming to introduce the liquid comprising water to the chamber, and the liquid adding flow line is used during priming to vent air from the chamber. During normal use, venting is not required.

[0074] Such a first type of chamber or partial dissolution chamber is suitable for containing sodium chloride or sodium bicarbonate for making the peritoneal dialysis fluid.

[0075] A second type of chamber is contemplated for other constituents of the peritoneal dialysis fluid, such as calcium chloride and magnesium chloride. In the case of these concentrates, they are generally only required in relatively small quantities and at low concentrations in the peritoneal dialysis fluid, and so a relatively small chamber can have an adequate volume such that one liquid fill will result in a sufficient amount of dissolved concentrate. Therefore, the apparatus may be arranged to prime ~~said~~the at least one concentrate in substantially dry form in a respective chamber with liquid comprising water, the amount of concentrate in the chamber and the size of the chamber being such that the concentrate is fully dissolved when the chamber is filled with liquid. With this type of chamber, the priming inflow can conveniently use the same flow line as that used to remove dissolved concentrate from the chamber. In the case of a rigid walled chamber, an air vent may be provided to vent air during priming and emptying.

[0076] A third type of chamber may be used for the osmotic agent, normally glucose. It is provided in substantially dry or solid e.g. powder form, and the apparatus will then be suitably equipped to stir, agitate or recirculate the glucose once liquid comprising water has been added. This is because of the relative difficulty in achieving rapid dissolution of glucose. In one embodiment of the apparatus, a respective chamber contains an osmotic agent, e.g. glucose, and the

apparatus comprises a flow circuit for introducing liquid comprising water into the osmotic agent chamber, for removing liquid comprising dissolved osmotic agent from the chamber and for re-introducing the liquid comprising dissolved osmotic agent into the chamber. Dissolution, e.g. of glucose, is generally promoted by heating the diluent liquid, for example to 40°C. Heated liquid may initially be supplied to the glucose chamber. It is desirable to maintain the glucose heated during dissolution and circulation, and advantageously therefore a heater is provided for heating the liquid comprising dissolved glucose as it circulates round the flow circuit.

[0077] Since glucose powder tends to release gas bubbles during dissolution, the apparatus may have a vent to allow escape of gas as the liquid comprising dissolved glucose circulates around the flow circuit.

[0078] The plurality of chambers containing respective concentrates may be provided by more than one container. It is, however, convenient for a user if all the ingredients for making the peritoneal dialysis fluid are provided in a single container. In one embodiment, the plurality of chambers are defined by a disposable container. In another embodiment, each chamber is in the form of a compartment of a container.

[0079] It will thus be appreciated that a plurality of different types of chambers may be provided to deal with the different requirements of the different constituents of the peritoneal dialysis fluid, i.e. taking account of the amount of each constituent normally required and the ease or difficulty in dissolving each constituent. From the user's perspective, however, there is the benefit that all the chambers and the constituents of the peritoneal dialysis fluid which they contain can be provided in a single container. This can provide all constituents needed for an overnight peritoneal dialysis treatment session, which may for example involve the use of from about 8- to 30 litres—liters of peritoneal dialysis fluid or more, without the user having to

set up the several bags of fluid which would be required with conventional peritoneal dialysis treatment.

[0080] It is possible to support the container on the apparatus in a fixed position and then for the apparatus to have a chamber communicating portion, e.g. a spike, which moves to a position communicating with the interior of a ~~said~~the chamber. In one embodiment, the apparatus comprises a container engaging portion for engaging the container and urging the container to a position in which the chambers are opened for communication with respective portions of the apparatus.

[0081] In general, it will be ~~desireable~~—desirable to place the container in a location where it can be engaged by the container engaging portion. One way of doing this is for a user to slide the container to the engagement location in a first direction, for example in a horizontal direction, and then for the container engaging portion to urge the container to the communicating position in a second direction, for example in a vertical direction.

[0082] The container engaging portion may, for example, engage a region of the container remote from the region of the chambers where they are to be opened. This may be the base of the container, inverted so that its opening region faces downwardly. In one embodiment, the container engaging portion is arranged to engage a plurality of flanges each provided adjacent to a respective opening of a respective chamber. By effecting engagement adjacent to the openings, reliable urging in the opening region of the container may be achieved. The flanges are, for example, formed on the necks defining the openings of the respective chambers.

[0083] In one embodiment, a flange associated with each opening is engaged, to ensure reliably and positively that each opening is communicated with the chamber communicating portions of the apparatus. It will be appreciated that it is important that all intended communicating paths should be created at the interface between the apparatus and the

container. In one exemplary container, there are eight chamber openings where communication is to be effected. One embodiment of the arrangement for achieving the desired reliable interface involves that at least two of the container openings being linearly aligned with each other, and the container engaging portion comprising a pair of laterally spaced members arranged to engage flanges defined on opposite sides of the openings.

[0084] In one embodiment of the apparatus, a plurality of spikes are provided for penetrating respective seals of the chambers to open ~~said~~the chambers. Each spike advantageously comprises two fluid flow channels, to allow simultaneous inflow and outflow of liquid or gas to or from the chamber. As will be apparent from the description below, in the case of a chamber containing glucose it is useful to provide three flow channels, whereas for other concentrates two channels are provided. Rather than having to provide a three flow channel spike, there is provided a pair of spikes for penetrating an osmotic agent, e.g. glucose, containing chamber. This can provide three flow channels, two contributed by one spike and the third by the other spike. In addition, since the osmotic agent chamber will usually be substantially larger than the other chambers, there will be sufficient space on the osmotic agent chamber wall for the provision of two openings.

[0085] After the container has been used to supply the ingredients for one or more peritoneal dialysis patient fills, it will be removed and on the next treatment occasion a fresh container will be used. It is beneficial to disinfect the spikes between treatments. The apparatus comprises a cover for covering a ~~said~~the spike when the container is removed to enable the spike to be disinfected. The container engaging portion may be arranged to engage the cover to urge it to its covering position. Thus, the container engaging portion can fulfil both the function of urging the container to its communicating position, and that of urging the cover to its covering position when no container is present.

[0086] It will be appreciated that the container described herein ~~itself~~-embodies a number of inventive aspects. A second aspect of the present invention is therefore concerned with a container, such as a disposable container.

[0087] In one form of the second aspect, the present invention provides a container containing, in concentrated form, all of the concentrates, which, when mixed with water, provide sufficient peritoneal dialysis fluid for a full peritoneal dialysis treatment session.

[0088] In another form of the second aspect, the present invention provides a container containing concentrated components of dialysis fluid, the container comprising a chamber containing powdered glucose and at least one other distinct chamber containing at least one powdered inorganic salt.

[0089] In another form of the second aspect, the present invention provides a container containing concentrated components of dialysis fluid, the container comprising at least one chamber containing a cleaning agent and at least one other distinct chamber containing at least one powdered inorganic salt. It is advantageous to provide a cleaning agent in the same container as at least one concentrate for making peritoneal dialysis fluid, as this facilitates operation of the apparatus, because the user is only required to insert one container into the apparatus to provide the concentrated PD fluid and to provide the cleaning agent, rather than separate containers which may be mistaken.

[0090] In another form of the second aspect, the present invention provides a container containing concentrated components of dialysis fluid, the container having defined therein at least two distinct chambers, each of ~~said~~the chambers containing a different inorganic salt, wherein the volume of each of ~~said~~the chambers and the amount of salt contained within each chamber is such that when a solution of each salt is prepared by filling each of ~~said~~the chambers with liquid, such as water, the conductivities of the solutions so

prepared are characteristically different. As described in more detail below, such an arrangement enables the apparatus with which the container is to be used to check that it is receiving the correct concentrate or inorganic salt from each chamber.

[0091] In another form of the second aspect, the present invention provides a container containing concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising at least one connector associated with each chamber, wherein each ~~said~~the connector comprises at least two separate fluid channels, permitting simultaneous inflow to and outflow from the respective chamber. This arrangement allows gas to exit the chamber via-through one fluid channel as liquid enters via-through the other fluid channel, and/or it allows gas to enter the chamber via-through one fluid channel as liquid exits via the other fluid channel, and/or it allows replacement liquid to enter the chamber as liquid exits the chamber. Such an arrangement is particularly useful in the case of chambers having relatively rigid rather than flexible (i.e. collapsible) walls, where the volume of the chamber remains substantially constant whether it is empty or full. By providing the at least two fluid channels as part of the connector, as distinct from providing a vent elsewhere on the chamber, the two fluid channels can be opened up and established only at the time when the container is to be used, such as simultaneously, for example by breaking a seal which may be in the form of a membrane or septum.

[0092] In one arrangement, the at least two fluid channels are arranged concentrically in each of ~~said~~the connectors. This type of connector can, for example, conveniently mate with a spike which itself has two fluid channels, as described above.

[0093] In the case of an osmotic agent, e.g. glucose, containing chamber, it is useful to have more than two fluid channels, notably three. In one embodiment, at least one of

saidthe chambers comprises two connectors, one such connector comprising saidthe at least two separate flow channels, and the other connector comprising a further fluid channel.

[0094] Again in the case of an osmotic agent, e.g. glucose, dissolution thereof can be advantageously promoted by providing one of the fluid channels with a diffuser to diffuse an inflow of liquid into the chamber.

[0095] In one embodiment, the connectors are provided, during operation, in a lower region of the chambers, and one of the fluid channels of at least one connector has a portion extending to an upper region of the chamber. The portion in the upper region can, for example, be used as an air vent, as an inlet for replacement liquid, or for recirculation.

[0096] As explained above, at least some of the openings to the chambers are in alignment with each other. ~~There~~Their openings are mutually aligned along the linear axis. Thus, the connectors can all be engaged by a container engaging portion of the apparatus. The connectors may comprise neck portions each formed with an external flange for engagement by the container engaging portion. A pair of flanges may be provided on opposite sides of the neck portion, or a single flange may extend circumferentially round the neck portion. The container engaging portion may then be in the form of a pair of laterally spaced members - a fork - for engagement with the flanges.

[0097] The container should be mountable on or insertable into the machine in a unique manner, to ensure that the correct connectors align with the required communicating portions of the apparatus. In one embodiment, the linear axis of the mutually aligned connectors is offset from a central axis of the container. The container can then interface with the apparatus in the correct manner only.

[0098] In another form of the second aspect of the present invention, there is provided a container for use in priming powdered glucose at a patient treatment location, comprising an inlet port in a lower region of the container for receiving

a supply of water to dissolve the powdered glucose in the container, wherein saidthe inlet port is provided with a diffuser which is arranged to diffuse the flow of water into the powdered glucose.

[0099] In another form of the second aspect of the present invention, there is provided a container for concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising at least one connector associated with each chamber, wherein at least two of saidthe connectors are mutually aligned along a linear axis.

[0100] In another form of the second aspect of the present invention, there is provided a container for concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising a container body and at least one connector associated with each chamber, wherein there is at least one axis about which the container body is substantially rotationally symmetric, and wherein the connectors are arranged relative to saidthe container body such that the arrangement of connectors is rotationally asymmetric about saidthe axis.

[0101] In the manufacture of the container, each chamber may be charged with the appropriate concentrate. It may be problematic to successively ~~to~~-charge each chamber of a single container. Therefore, the container may be made as a plurality of sub-containers which are later connected together.

[0102] In another form of the second aspect of the present invention, the invention provides a method of manufacturing a container for concentrated components of dialysis fluid, the method comprising the steps of:

manufacturing a plurality of individual sub-containers; and
connecting saidthe sub-containers to form saidthe container.

[0103] The present invention also extends to a container made by the above method.

[0104] The apparatus may be connected to a source of

purified water, for example a reverse-osmosis unit. In one embodiment, the apparatus comprises a water purifier. The water purifier may, for example, comprise one or more reverse osmosis membrane units. In one embodiment, the water purifier comprises a first reverse osmosis membrane unit, and a second reverse osmosis membrane unit. Each membrane unit has an inlet, a purified water outlet and a waste water outlet. In one embodiment, the purified water outlet of the first membrane unit is in fluid communication with the inlet of the second membrane unit. Moreover, the waste water outlet of the second membrane unit may be in fluid communication with the inlet of the first membrane unit.

[0105] According to this arrangement, the water from the waste water outlet of the second RO membrane unit, which is already reasonably pure because it has been through the first RO membrane unit, is recycled and passes through the first RO membrane unit again, so that the overall water consumption of the apparatus is reduced. In this way, two RO membrane units can be used, in order to ~~give~~provide a higher purity of water, without increasing the overall water consumption of the apparatus.

[0106] The water purifier may comprise, for example upstream of the inlet of the RO membrane unit, a coarse filter (for example a 30 micron filter), a fine filter (for example a 5 micron filter), a charcoal filter and/or a water softener. Each of these components prevents blocking of the reverse osmosis membranes.

[0107] The water purifier may further comprise a degassing arrangement upstream of the first (or second) RO membrane unit. The water is degassed before it passes through the RO membranes, as a reduction in the amount of dissolved carbon dioxide and other gases in the water can improve the performance of the RO membrane(s). Furthermore, gas bubbles in the water can interfere with the correct operation of the pumps and the like. In general, it is desirable for the water to be degassed at an early stage in the production of the

peritoneal dialysis fluid, as this simplifies the further processing steps, because the dissolved gas content of the water is fixed.

[0108] In one embodiment, the ~~steriliser~~sterilizer is a heat ~~steriliser~~sterilizer.

[0109] Viewed from a third aspect, the present invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location comprising:

a water inlet for receiving a supply of water from a mains water supply;

a water purifier for purifying the supply of water from the water inlet;

a fluid mixer for mixing dialysis fluid concentrate with the purified water supply to produce a supply of peritoneal dialysis fluid;

a ~~steriliser~~sterilizer for ~~sterilising~~sterilizing the supply of peritoneal dialysis fluid; and

a fluid outlet arranged to communicate the ~~sterilise~~sterilized supply of peritoneal dialysis fluid to the peritoneal cavity of a patient; and further wherein
~~characterised in that~~

the ~~steriliser~~sterilizer is a heat ~~steriliser~~sterilizer arranged for heat ~~sterilisation~~sterilization of the peritoneal dialysis fluid at a ~~sterilising~~sterilizing temperature and at an elevated pressure.

[0110] Heat ~~sterilisation~~sterilization is generally considered to be effective and safer than, for example, bacterial filtering.

[0111] In one embodiment, the ~~steriliser~~sterilizer is provided downstream of the fluid mixer so that any bacteria introduced into the peritoneal dialysis fluid during mixing are neutralised. In this way, the production costs of the container for the concentrated components can be reduced, because the components need not be pre-~~sterilise~~sterilized.

[0112] Although the ~~steriliser~~sterilizer may be configured to ~~sterilise~~sterilize the peritoneal dialysis fluid itself,

alternatively one or more ~~steriliser~~sterilizers may be provided for ~~sterilising~~sterilizing one or more of the components of the peritoneal dialysis fluid, such as the liquid, for example water, used to form the peritoneal dialysis fluid and/or the concentrated solutions. If the concentrates are provided as sterile concentrates, only the water used to form the peritoneal dialysis fluid is ~~sterilise~~sterilized.

[0113] The ~~steriliser~~sterilizer may comprise a ~~sterilisation~~sterilization flow passage and is arranged to heat ~~sterilise~~sterilize the peritoneal dialysis fluid as it flows along the ~~sterilisation~~sterilization flow passage, so that the flow of peritoneal dialysis fluid does not need to be stopped for heat ~~sterilisation~~sterilization. In one embodiment, the apparatus comprises a flow path downstream of the heat ~~steriliser~~sterilizer for the flow of ~~sterilise~~sterilized peritoneal dialysis fluid to the patient fill connection, and cooling means for cooling the ~~sterilise~~sterilized peritoneal dialysis fluid as it flows along the flow path, in order that the peritoneal dialysis fluid may be brought to body temperature when it reaches the patient fill connection. The apparatus may be arranged to heat ~~sterilise~~sterilize the flow path prior to its use for the flow of ~~sterilise~~sterilized peritoneal dialysis fluid to the patient fill connection, to ensure that the ~~sterilise~~sterilized fluid travels along a ~~sterilise~~sterilized path.

[0114] A fourth aspect of the present invention is concerned with systems for dissolving a substantially dry concentrate and delivering the dissolved concentrate to a mixing vessel.

[0115] Viewed from a fourth aspect therefore the present invention provides apparatus for the production of an aqueous solution for medical use from a plurality of concentrates, the apparatus being arranged to communicate with a plurality of chambers each containing a respective concentrate, at least

one of the concentrates being in substantially dry form, the apparatus comprising:

at least one flow line arranged to prime ~~said~~the at least one concentrate in substantially dry form with liquid comprising water to form at least one dissolved concentrate;

a mixing vessel arranged to receive the at least one dissolved concentrate;

a flow regulator associated with the at least one dissolved concentrate arranged to pass the concentrate to the mixing vessel; and further comprising

~~characterised by~~

measuring means arranged to measure a concentration of the at least one dissolved concentrate; and

a pump arranged to pump a metered volume of the at least one dissolved concentrate ~~via~~ by means of the associated flow regulator to ~~said~~the mixing vessel, ~~while~~ while measuring by ~~said~~the measuring means the concentration of the dissolved concentrate, so as to deliver a predetermined amount of ~~said~~the dissolved concentrate to ~~said~~the mixing vessel.

[0116] The present invention also provides a method ~~or of~~ providing an aqueous solution for medical use from a plurality of concentrates, comprising:

providing a plurality of concentrates in separate chambers, at least one of the concentrates being in substantially dry form; priming ~~said~~the at least one concentrate in substantially dry form with liquid comprising water to form at least one dissolved concentrate;

passing the at least one dissolved concentrate to a mixing vessel ~~via~~ by means of a flow regulator associated with that concentrate; and further including

~~characterised by~~

adjusting the flow regulator associated with the at least one dissolved concentrate for passing a metered volume of ~~said~~the concentrate through ~~said~~the flow regulator;

measuring a concentration of ~~said~~the concentrate to determine an amount of ~~said~~the concentrate delivered to ~~said~~the mixing

vessel; and

terminating ~~said~~the delivering of concentrate when a predetermined amount has been delivered.

[0117] Thus, from a starting point of concentrates at least one of which is in substantially dry form, e.g. powder, ~~form~~, an aqueous solution may be obtained in a mixing vessel comprising a predetermined amount of each concentrate, and hence having each concentrate present in a predetermined concentration ratio. Such solution can be prepared to a precise desired formulation, and may be put to medical use, for example for the purposes of peritoneal dialysis, hemodialysis, hemofiltration or hemodiafiltration.

[0118] In general, it is intended to obtain a flow of concentrate at a predetermined concentration and this may take time to develop, for example because time is required to achieve dissolution or because adjustments are made e.g. dilution to achieve a flow at the predetermined concentration. It is beneficial to use the flow as soon as it is established at the desired concentration, rather than to send it to drain ~~whilst~~while awaiting a similar establishment for another concentrate. By providing a mixing vessel in which a known amount of concentrate is to be stored, that concentrate can be passed to the mixing vessel without delay and thus without significant loss to drain.

[0119] Where a plurality of concentrates are provided in substantially dry form, each such concentrate is primed to form a dissolved concentrate, a metered volume of each dissolved concentrate is pumped via-by means of its associated valve to the mixing vessel, ~~whilst~~while measuring the concentration of the dissolved concentrate, so as to deliver a predetermined amount of the dissolved concentrate to the mixing vessel. Thus, an aqueous solution is obtained comprising a predetermined amount of each concentrate.

[0120] Where one or more concentrates are initially provided in liquid form, they may be provided at a known concentration, in which case the concentration measuring step

may not be necessary, it being sufficient to pump a metered volume to the mixing vessel. However, to be sure of obtaining the right amount of all concentrates in the mixing vessel, it is possible to measure the concentration of such initially liquid concentrates as they are passed to the mixing vessel. This would also be useful where a concentrate is provided initially in liquid form at a concentration which is only approximate. An example of a concentrate which may be provided in liquid form to make e.g. peritoneal dialysis fluid is lactic acid.

[0121] Another method therefore comprises adjusting a first flow regulator associated with a first concentrate for passing the first concentrate through the first flow regulator at a metered rate, measuring a concentration of the first concentrate to determine an amount of ~~said~~the concentrate delivered to ~~said~~the mixing vessel, terminating ~~said~~the delivering of ~~said~~the first concentrate when a predetermined amount has been delivered, adjusting a second flow regulator associated with a second concentrate for passing the second concentrate through the second flow regulator at a metered rate, measuring a concentration of the second concentrate to determine an amount of ~~said~~the concentrate delivered to ~~said~~the mixing vessel, terminating ~~said~~the delivering of ~~said~~the second concentrate when a predetermined amount has been delivered, and repeating ~~said~~the adjusting, passing, measuring and terminating for each further concentrate, thereby to provide an aqueous solution comprising a predetermined amount of each concentrate. Such a method is applicable to a plurality of concentrates in which at least one is provided in substantially dry form, i.e. there may initially be ~~plural~~ a plurality, one or no concentrates provided in liquid form. To make dialysis fluid, for example, the electrolytes and osmotic agent may be provided as solid concentrates, e.g. powders, ~~whilst~~ while an acid may be provided as a liquid concentrate.

[0122] In one embodiment, the apparatus comprises a flow

regulator associated with each concentrate, wherein in use of the apparatus a metered volume of each concentrate is pumped via-by means of its associated valve to the mixing vessel, whilst-while measuring the concentration of the concentrate, so as to deliver a predetermined amount of the concentrate to the mixing vessel. For example, there may be a first flow regulator associated with a first concentrate, a second flow regulator associated with a second concentrate, and a further flow regulator associated with each further concentrate.

[0123] The pumping of concentrate flows may be effected by a plurality of devices, such as metering pumps, for example one associated with each concentrate. In one embodiment, the pump is arranged for pumping, in turn, each concentrate to the mixing vessel. Thus, the use of a pump associated with each concentrate can be avoided, thereby reducing the cost, size and weight of the system, particularly where several concentrates are involved, as will be the case for dialysis liquids, for example.

[0124] Similarly, although a plurality of concentration measuring means may be provided, again one associated with each concentrate, each concentrate may alternatively be passed via-through the same measuring means. This may reduce the cost, size and weight of the system. In addition, because the measuring means measures the concentration of each concentrate individually, it can be selected or set up to give accurate measurements over a range wide enough to cover the expected individual concentrations. This is intended in a system in which a measuring means is used to measure e.g. the conductivity of the solution accumulating in the mixing vessel, since the conductivity will increase as additional concentrates are added and the measuring means would then be required to be accurate over a wide range, i.e. a range sufficient to cover the conductivity of a first concentrate, the higher conductivity of a first and second concentrate combined, etc. Furthermore, in such a cumulative system, measurement errors resulting from the measurement of the first

concentrate will add to the errors in the measurement of the second concentrate and so on, so that later concentrates are measured at a lower accuracy than initial ones. This does not occur when the concentration of each concentrate is measured individually as the errors are due only to the measurement being taken.

[0125] The measuring means may comprise more than one measuring device, such as two measuring devices, to provide the system with redundancy and thus additional safety. The measuring means may comprise a pH meter or other type of meter, such as an ion selective meter, but preferably comprises a conductivity meter.

[0126] The apparatus may be arranged to dilute a concentrate after it leaves its respective chamber and before it is passed to the mixing vessel. By controlling the amount of dilution, the concentration of the constituent substance delivered to the mixing vessel can be controlled to a predetermined concentration, even starting from different predilution concentrations, which may often be the situation in the case of a concentrate initially provided in substantially dry form. The dilution may for example be effected by a proportioning pump. In one dilution arrangement, it comprises a concentrate flow line along which concentrate is pumped by the pump at a metered rate, a water flow line along which water is pumped by a second pump at a metered rate, the concentrate flow line joining the water flow line so that in use the concentrate and water are mixed to dilute the concentrate before it is passed to the mixing vessel. The concentration of the concentrate or diluted concentrate is measured, and the pumps are controlled to provide a dilution ratio required in order to obtain a desired concentration of the diluted concentrate.

[0127] A convenient method of achieving the delivery of a predetermined amount of concentrate to the mixing vessel comprises passing ~~said~~the diluted concentrate to the mixing vessel at a flow rate, measuring the concentration of the

diluted concentrate, multiplying ~~said~~the measured concentration with ~~said~~the flow rate, integrating the product of ~~said~~the multiplication over time to obtain a total amount of concentrate material delivered to ~~said~~the mixing vessel, and terminating ~~said~~the passing of diluted concentrate to ~~said~~the mixing vessel when a predetermined amount of concentrate material has been delivered to ~~said~~the mixing vessel. The apparatus may therefore include a suitable processor for carrying out the multiplying, integrating and terminating functions.

[0128] The plurality of chambers containing concentrates will normally be provided in predetermined positions relative to each other and relative to the apparatus to ensure that each concentrate is supplied to the appropriate portion of the apparatus. In one embodiment, the apparatus is able to check that it has received the correct concentrate at each appropriate portion. Therefore, the method comprises measuring a property of a ~~said~~—concentrate or a property of the concentrate after dilution thereof downstream of its respective chamber, and determining from that measurement if the concentrate is the concentrate expected from that chamber.

[0129] ~~Whilst~~—While the measured property may be pH, for example, it may be difficult to distinguish between concentrates which have a neutral pH at any concentration. In one embodiment, the measured property is conductivity. The concentrates may be provided in amounts in their respective chambers such that when their properties e.g. conductivities are later measured they are distinguishable from each other. The property may be measured in its form as supplied from the chamber, i.e. without further dilution. If it is measured after dilution, then providing dilution is effected by the addition of a known amount of liquid comprising water, then the measurement for the expected concentrate can still be known.

[0130] The concentration of the concentrates in the mixing vessel may provide the final formulation for the required

medical use. However, in order that the mixing vessel can be kept to a reasonable size, in one embodiment, the liquid in the mixing vessel is passed towards a point of use and to dilute the liquid downstream of the mixing vessel.

[0131] Dilution can be effected by feeding liquid from the mixing vessel into a water conducting line, the mixing vessel liquid being pumped at a known rate and the diluted liquid being pumped at a higher known rate, whereby water is drawn from a source at a flow rate being the difference between the known flow rate of the mixing vessel liquid rate and the known flow rate of the diluted liquid. Thus, the extent of dilution will be known. In order to be sure to ~~obtaining~~ obtain the correct formulation for the diluted liquid, having regard to its medical use e.g. as peritoneal dialysis fluid, it is also ~~checked~~ ensured that the extent of dilution is correct. This may be achieved by providing a suitable measuring means, such as conductivity measuring means. The cost, size and weight of the apparatus may be minimised by measuring the concentration of the concentrates in the diluted liquid downstream of the mixing vessel using the same measuring means as is used to measure the concentration of the concentrates during delivery to the mixing vessel.

[0132] Where a common flow path is used at some point downstream of the valve associated with each concentrate, it may be desirable to flush that path (or part thereof) after delivery of one concentrate and before delivery of the next. In one arrangement, the pump is reversible and connectable to a source of liquid, such that in use of the apparatus, after termination of delivery of a ~~said~~ the concentrate, the pump is reversed to pump ~~said~~ the liquid from the source thereof through the associated flow regulator so as to flush the path between the liquid source and the flow regulator, such as a valve. The liquid used for flushing is preferably water.

[0133] It will be appreciated from the foregoing that the system for producing different medical formulations at a treatment location involves a further inventive aspect. A

fifth aspect of the present invention is therefore concerned with such a system.

[0134] In one form of the fifth aspect, the present invention provides apparatus for use at a treatment location which uses a plurality of concentrates and is able to produce from those concentrates a range of different peritoneal dialysis fluid formulations, each such formulation being based on predetermined prescription information and comprising at least one of the concentrates in diluted form.

[0135] Such an apparatus is an advance over the known systems for peritoneal dialysis involving the use of a range of pre-prepared formulations, which are made remotely from the treatment location and must then be selected according to the required formulation and transported to the treatment location. Rather, the plurality of concentrates is used by the apparatus to make up the required formulation on site, according to prescription information determined by a physician or other qualified medical professional. This simplifies inventory control for the manufacturer, who no longer has to produce a range of different pre-prepared formulations, but instead can supply the plurality of concentrates. This is also more convenient for the physician and the patient, who no longer need to concern themselves with ensuring that they are supplied with the right pre-prepared bags of fluid.

[0136] In another form of the fifth aspect, the present invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:
a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid;
a fluid mixer arranged to mix the concentrates with liquid to produce peritoneal dialysis fluid;

a controller arranged to control the fluid mixer selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other;

a ~~steriliser~~sterilizer arranged to ~~sterilise~~sterilize at least one of the liquid and the peritoneal dialysis fluid; and a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal cavity of a patient₇; and further wherein
~~characterised in that~~

the controller has data input means for receiving predetermined prescription information for a patient and in ~~that~~ the controller is operable to control the fluid mixer to produce a peritoneal dialysis fluid formulation based on the received predetermined prescription information.

[0137] Thus, the plurality of concentrates can be used to make the formulation required by a patient and based on a prescription determined in advance of treatment. There is no need to use a different set of concentrates for each formulation, and accordingly no need to have a required set of concentrates delivered to the treatment location. The prescribing process is separated from the delivery process, giving medical practitioners greater freedom to vary a prescription e.g. from one treatment to the next. Because of the greater flexibility in prescribing which is provided, it may be possible to keep some patients on peritoneal dialysis treatment for longer before they have to be switched to hemodialysis treatments.

[0138] In one embodiment, the chambers are in the form of compartments of a container and all the concentrates required to make a ~~said~~the peritoneal dialysis formulation are provided in ~~said~~the compartments. Thus, a single container of concentrates can be used to make a range of different formulations, again simplifying use of the system for medical ~~practitioners~~practitioners and for patients.

[0139] The concentrates may comprise a plurality of electrolytes and the controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative electrolyte concentrations from each other. Thus, a medical practitioner can vary the relative electrolyte

concentrations to take account of a patient's surplus or shortage of certain salts or ions. Again, this can be done without concern for what pre-prepared bag or bags of formulations are available for use at the treatment location.

[0140] In a further form of the fifth aspect, the present invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising: a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid; a fluid mixer arranged to mix the concentrates with liquid to produce the peritoneal dialysis fluid; a controller arranged to control the fluid mixer selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other; a ~~steriliser~~sterilizer arranged to ~~sterilise~~sterilize at least one of the liquid and the peritoneal dialysis fluid; and a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal dialysis of a patient; and further wherein ~~characterised in that~~

the concentrates comprise a plurality of electrolytes, and in ~~that~~ the controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative concentrations of electrolytes.

[0141] The advantages of such apparatus will be apparent from the discussions above and below.

[0142] It is to be understood that both the foregoing general description and the following detailed description are exemplary and are intended to provide further explanation of, without limiting the scope of, the invention as claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0143] ~~An embodiment~~ Embodiments of the present invention will now be described by way of example only, and with reference to the following detailed description which, in turn, refers to the accompanying drawings, in which ~~are~~

~~incorporated in and constitute a part of the specification. In the drawings:~~

[0144] Figure 1 is a front, perspective, partially schematic perspective-view of an apparatus for the preparation of peritoneal dialysis fluid according to ~~an one~~ embodiment of the present invention;

[0145] Figure 1a is a block diagram of a processor system in the apparatus of figure 1;

[0146] Figure 2 is a schematic view-representation of a fluid path in the apparatus of Figure 1, in terms of interconnected functional modules;

[0147] Figure 3 is a detailed schematic view-representation of a water preparation module of Figure 2;

[0148] Figure 4 is a detailed schematic view-representation of a thermal control and ~~sterilisation~~ sterilization module of Figure 2;

[0149] Figure 4a is a detailed schematic view representation of an alternative embodiment of the thermal control and ~~sterilisation~~ sterilization module of Figure 4 ~~in an alternative arrangement~~;

[0150] Figure 5 is a detailed schematic view-representation of a concentrate mixing module of Figure 2;

[0151] Figure 5a is a detailed schematic view representation of an alternative arrangement-embodiment of the concentrate mixing module of Figure 2;

[0152] Figure 5b is a detailed schematic view representation of an alternative arrangement-embodiment of the concentrate mixing module of Figure 5a;

[0153] Figure 6 is a detailed schematic view-representation of a drainage module of Figure 2;

[0154] Figure 7 is a detailed schematic view-representation of a cycler and ~~sterilisable~~ sterilizable connector module of Figure 2;

[0155] Figure 8 is a front perspective view-representation of a first example of a heat exchanger for use in the ~~sterilising~~ sterilizing of PD fluid according to

the present invention;

[0156] Figure 9 is a front, perspective view of a second example—embodiment of a heat exchanger for use in the sterilisingsterilizing of PD fluid according to the present invention;

[0157] Figure 10 is a side, perspective view of a disposable concentrate container according to the present invention;

[0158] Figure 11 is a side, elevational, partially sectional view through the disposable concentrate container of Figure 10 with a vertical section of a chassis removed;

[0159] ~~Figures—Figure 12a to 12c are~~ is a side, perspective views—view of portions—a portion of the disposable concentrate container of Figure 10;

[0160] Figure 12b is a bottom, perspective view of another portion of the disposable concentrate container of Figure 10;

[0161] Figure 12c is a top, perspective view of another portion of the disposable concentrate container of Figure 10;

[0162] Figure 13 is a front, perspective view of a compartment of the disposable concentrate container of Figure 10;

[0163] Figure 14 is a front, perspective view of a further compartment of the disposable concentrate container of Figure 10;

[0164] Figure 15 is a side, elevational, sectional view through the disposable concentrate container of Figure 10 during fitting to the apparatus of the present invention;

[0165] Figure 16 is a ~~further side, elevational, exploded,~~ sectional view through the disposable concentrate container of Figure 10 during fitting to the apparatus of the present invention;

[0166] Figure 17 is a side, elevational, sectional view through the disposable concentrate container of Figure 10 in position on the apparatus of the present invention;

[0167] Figure 18 is ~~an alternative—~~ a side, elevational, sectional view of an alternative embodiment of the disposable

concentrate container of Figure 10;

[0168] ~~Figures—Figure 19a–19d—~~are is a side, elevational, schematic views—view of a ~~sterilisable~~sterilizable connector of the apparatus of the present invention;

[0169] Figure 19b is a side, elevational, sectional view of a sterilizable connector of the apparatus of the present invention;

[0170] Figure 19c is a side, elevational, sectional view of a sterilizable connector of the apparatus of the present invention;

[0171] Figure 19d is a side, elevational, sectional view of a sterilizable connector of the apparatus of the present invention;

[0172] Figure 20 is a top, elevational, schematic view of a disposable fluid line for use with the apparatus of the present invention;

[0173] Figure 21 is a top, elevational, schematic view of a sampling disposable fluid line for use with the apparatus of the present invention;

[0174] Figure 22 is a ~~detailed—side, elevational, partial, sectional partial—~~view of a compartment of the disposable concentrate container of Figure 10;~~—and~~

[0175] Figure 23 is a side, elevational, sectional view through a glucose compartment of the disposable concentrate container of Figure 10.

[0176] Figure 24 is a side, elevational, sectional view through a lactic acid compartment of the disposable concentrate container of Figure 10—; and

[0177] Figure 25 is a side, elevational, sectional view through the lactic acid compartment of Figure 24 in an engaged position.

~~Description of the detailed embodiments~~DETAILED DESCRIPTION

[0178] Referring to the Figures, in which like reference numerals refer to like elements thereof, Figure 1 is a partially schematic perspective view of an apparatus 100 for the preparation of peritoneal dialysis fluid for a patient

according to a first embodiment of the present invention. The apparatus 100 is connected to a domestic water supply by means of a tap water connection 1 and is connected to the domestic sewerage system by means of an external drain connection 16. The external waste connection 16 may be in the form of a replaceable waste line. The apparatus 100 is powered by the domestic electricity supply ~~via~~by means of a mains electricity connection 20. Concentrated components of the PD fluid are supplied to the apparatus 100 in a concentrate disposable container 402. The PD fluid is supplied to and drained from the patient's peritoneal cavity by a disposable fluid line 10 which forms a fluid connection between the patient and the apparatus 100.

[0179] The apparatus 100 receives details of a prescription of the PD fluid for the patient on a smart card 102 which is read by the apparatus 100. The apparatus 100 also includes a control panel 104 which displays information to the patient and allows the patient to control the operation of the apparatus in certain respects.

[0180] In overview, the apparatus 100 according to this embodiment of the present invention is installed in a patient's home and purifies tap water from the tap water connection 1, mixes the purified tap water with concentrated PD fluid components from the concentrate disposable container 402 to produce PD fluid. The apparatus 100 then ~~sterilises~~sterilizes the PD fluid and delivers the PD fluid by way of the disposable fluid line 10 directly to the peritoneal cavity of the patient. During a treatment session, which comprises a series of fill and drain cycles, old PD fluid, dialysate, is removed and fresh PD fluid is added to the patient's peritoneal cavity, normally during the night while the patient is asleep.

[0181] The disposable container 402 may include a bar code 18 arranged on the container at a convenient position. A bar code reader 19 shown in broken lines, inside the apparatus 100 reads the bar code as the container is inserted in the

apparatus.

[0182] Although the apparatus 100 is primarily intended for use in a patient's home, the apparatus 100 may be used in ~~centres~~centers such as dialysis clinics and hospitals. The apparatus includes a control system (not shown) which monitors and controls the operation of the apparatus 100 during normal use. In addition to the control system, the apparatus 100 includes a protective system (not shown) which is separate from the control system and monitors the correct operation of the apparatus 100 independently of the control system to ensure that the patient's safety is not compromised. The control system and the protective system are able to carry out functional tests to ensure that they are operating correctly.

[0183] At the start of the treatment session, the user, for example the patient, is required to confirm some of the parameters of the intended treatment which are displayed on the control panel 104. Such parameters include, for example, the patient's name, the volume of PD fluid to be entered into the peritoneal cavity of the patient, the glucose concentration of the PD fluid or the ~~expiry~~expiration date of the disposable concentrate container 402. Some of these parameters are stored on the smartcard 102. This corresponds to the stage in traditional PD treatments where the patient compares the label on the plastic bag of PD fluid with the instructions given by the doctor. Also, at the start of the PD treatment, the patient is required to identify himself to ensure that the apparatus is not operated by an unauthorised person.

[0184] At the end of a treatment session, the concentrate disposable container 402 is replaced and the old container is discarded. Similarly, the disposable fluid line 10 is also replaced at the end of the treatment session with a new line.

[0185] At the start of a treatment session, the patient can set the concentration of glucose required in the PD fluid for that treatment session, within predefined limits, according to the patient's requirements. The glucose concentration is set

by the patient using the control panel 104. The glucose in the PD fluid acts as an osmotic agent, so that an increase in the glucose concentration will result in an increase in the volume of fluid drawn across the peritoneum of the patient during the PD treatment.

[0186] The apparatus 100 is suitable for continuous cycling peritoneal dialysis (CCPD), where the peritoneal cavity is filled and emptied of PD fluid in a cyclic sequence, usually during the night. The apparatus 100 is also capable of carrying out tidal peritoneal dialysis according to which the peritoneal cavity is initially filled with PD fluid and in subsequent cycles a volume less than the total volume of the initial fill is drained from the peritoneal cavity and replaced with an approximately equal volume of fresh fluid. The peritoneal dialysis treatment session may take place while the patient is asleep and thus the apparatus 100 is usually located adjacent the patient's bed. Other treatment modes are also possible.

[0187] At the end of a treatment session, the peritoneal cavity of the patient may be left full of PD fluid or the PD fluid may be drained from the peritoneal cavity, depending on the patient requirements. In general, it is expected that the apparatus 100 will be the sole source of the patient's PD treatment. Thus, if at the end of a treatment session the patient's peritoneal cavity is full of PD fluid, it is expected that the cavity will be full of PD fluid at the beginning of the next treatment session. However, the patient may have drained or filled his peritoneal cavity manually using additional PD equipment between treatment sessions. The apparatus 100 is able to respond to such situations by having input means whereby the patient may enter relevant data to the apparatus.

[0188] In a usual treatment session, a total volume of about 8-25 litres of PD fluid is put into and removed from the patient's peritoneal cavity, with each fill volume being between 250 ml and 3 litres (the smaller volume may be in the

case of tidal peritoneal dialysis, for example). One treatment session may involve up to 20 fill and drain cycles, with a maximum of 25 litres of PD fluid (50 litres if the disposable concentrate container 402 is changed) being supplied to the patient and a maximum of 35 litres of fluid (per container used) being drained from the patient, the drain volume being up to 4 litres per cycle.

[0189] The patient is able to instruct the apparatus 100 via-by means of the control panel 104 to abandon the treatment session and allow the patient to disconnect from the apparatus 100 or to finish the treatment session early by omitting some of the cycles within the treatment session.

[0190] The apparatus 100 includes a timer (not shown) which allows the patient to set the approximate time at which a treatment session should begin so that the apparatus 100 can make the necessary preparations for the treatment session before the patient arrives. Thus, when such a time has been set, treatment can begin less than 20 minutes, preferably less than 10 minutes, after the patient has arrived and has confirmed that a treatment session is actually required. If the timer has not been preset, the apparatus 100 may require up to one hour to make the necessary preparations for the delivery of dialysis fluid.

[0191] The control panel 104 includes a 256 colour video touch screen display with a screen saver. The control panel allows the user, *inter alia*, to set the glucose level concentration of the PD fluid within preset limits, start, interrupt, resume, abandon or finish the treatment session, adjust the temperature of the dialysis fluid between 35°C and 40°C and set the planned start time for the next or subsequent treatment sessions. The control panel displays the treatment status and the time until the end of the treatment session during treatment or the time until the start of the treatment session during preparation for a treatment session. On request, the control panel 104 displays the treatment mode (for example tidal or continuous peritoneal dialysis), the

number of cycles in the treatment session, the glucose concentration, the accumulated fill volume for the treatment session, the accumulated drain volume for the treatment session, the accumulated ultrafiltration volume for the treatment session, the fluid delivery temperature set point, patient identification information from the smartcard 102 or patient entered information, the status of the treatment session and technical error codes. The ultrafiltration volume is the difference between the volume of PD fluid supplied to the patient and the volume of PD fluid drained from the patient. The control panel is also able to display visual alarms and is provided with an audible alarm with which the apparatus 100 can bring the patient's attention to operating problems. The control panel 104 may also be arranged to display additional information for use by a nurse, such as service information and fill rates and volumes, provided that the nurse can provide a valid identification code.

[0192] The apparatus 100 can be interrogated by a service engineer using a laptop computer (not shown) either directly or via a remote connections such as a modem (not shown).

[0193] The smartcard 102 stores the patient's prescription and for each of the last 20 treatment sessions, the prescription, the ultrafiltration volume, the monitor identity, date and time plus any variances between the prescribed and delivered treatment and the reasons therefor if known to the monitor. The smartcard 102 also stores patient identification information and the acceptable limits of patient-selected levels such as numbers of cycles and glucose concentration. The physical characteristics of the smartcard are similar to those used in the PD 200™ peritoneal dialysis system manufactured by Gambro AB of Lund, Sweden, although the apparatus 100 can differentiate between the PD 200 cards and cards suitable for use with the apparatus 100.

[0194] The information on the smartcard 102 can be altered by a doctor either by connecting a computer (not shown) with a suitable interface to the apparatus 100 or by inserting the

smartcard 102 into a suitable card reader attached to a computer (not shown). Service personnel are also able to interrogate the apparatus 100 using a computer (not shown) and a data link directly to the apparatus.

[0195] Figure 1a shows a block diagram of a smart card reader 103 which is connected to an operating system processor 108 and a protective system processor 106. The processors operate and supervise the system in a manner previously known in the art of dialysis machines. The processors are also connected to the control panel 104. Processors 106 and 108 are associated with memory devices 110 and 112, such as volatile memory, static memory, hard disk, solid state memory devices etc.

[0196] The operating system processor receives data input from sensors and other means in the apparatus and output control signals for controlling processes in the apparatus such as valves and pumps.

[0197] The protective system processor receives data input from sensors and other means in the apparatus and output control signals for the purpose of supervising the operating system processor and other processes in the apparatus. The protective system sensors are separate from the operating system processor sensors.

[0198] Figure 2 shows schematically the fluid path in the apparatus 100 of Figure 1. The apparatus is, for ease of understanding, represented in terms of six interconnected functional modules, which each perform a specific role in the preparation of the peritoneal dialysis fluid and the peritoneal dialysis treatment. These modules are: a water preparation module 200; a thermal control and ~~sterilisation~~sterilization module 300; a concentrate mixing module 400; a drainage module 500; a cycler and ~~sterilisable~~sterilizable connector module 600; and a sampling module 700.

[0199] In the following, the overall structure of the fluid path in the apparatus 100 will be described and then further

details of the individual modules will be given.

[0200] As used in this description the terms "cleaning", "disinfection" and "~~sterilisation~~sterilization" have distinct meanings: "cleaning" simply means the removal of deposits within the system; "disinfection" means the neutralisation of most bacteria; and "~~sterilisation~~sterilization" means the inactivation of all bacteria with a 1 in 10^6 confidence level, i.e. the theoretical probability of the presence of a viable microorganism is less than or equal to 10^{-6} (see United States Pharmacopoeia, 23rd Edition and European Pharmacopoeia 1997).

[0201] As shown in Figure 2, tap water from the domestic supply is provided to the water preparation module 200 by means of the tap water connection 1. The water preparation module 200 controls the supply of water to the other modules in the apparatus by switching the tap water supply on and off, by limiting the pressure of the water supply and by monitoring the availability of the water supply. The water preparation module 200 also reduces and controls the level of dissolved gas and chemical and bacteriological contamination in the water supplied to the concentrate mixing module 400. The water preparation module 200 is capable of operating with potable water as generally defined by the US Environmental Protection Agency in the drinking water standard of November 1996, at pressures from 1-6 bar gauge (100-600 kPa above atmospheric pressure) and at temperatures between 5 and 30°C.

[0202] The water preparation module 200 is connected to the thermal control and ~~sterilisation~~sterilization module 300 by means of five fluid connections 2a-2e. A cooling water output connection 2a supplies softened, pressure-controlled water for use in the cooling functions of the thermal control and ~~sterilisation~~sterilization module 300. The temperature of the cooling water is raised in the thermal control and ~~sterilisation~~sterilization module 300, due, at least in part, to the water being used for cooling purposes. In this way, the water returned to the water preparation module 200 is preheated to improve the efficiency of the water preparation

module, using waste heat from other parts of the apparatus 100. The cooling water is returned to the water preparation module 200 from the thermal control and ~~sterilisation~~sterilization module 300 ~~via~~through a cooling water return connection 2b at a controlled temperature of approximately 30°C.

[0203] Purified water prepared by the water preparation module 200 is passed to the thermal control and ~~sterilisation~~sterilization module 300 ~~via~~by means of a purified water connection 2c. Waste water from the water purification process is passed from the water preparation module 200 to the thermal control and ~~sterilisation~~sterilization module 300 for cooling ~~via~~by means of a purification waste connection 2d.

[0204] The water preparation module 200 vents excess gas to atmosphere ~~via~~through an isolator air vent 17. The water preparation module 200 is also able to vent air to and from the thermal control and ~~sterilisation~~sterilization module 300 ~~via~~through a patient heat exchanger vent connection 2e.

[0205] For disinfection purposes the water preparation module 200 receives water at disinfection temperature from the concentrate mixing module 400 ~~via~~by means of a reverse osmosis (RO) membrane disinfection connection 3.

[0206] The water preparation module 200 has a connection for a disinfectant cartridge 210, which supplies chemical disinfectant for the disinfection of the water preparation module 200, when required.

[0207] The thermal control and ~~sterilisation~~sterilization module 300 ~~sterilise~~sterilizes the PD fluid supplied to the patient, and provides a supply of sufficiently hot water for disinfection of the concentrate mixing module 400 and the drainage module 500.

[0208] The thermal control and ~~sterilisation~~sterilization module 300 also controls the temperature of the water supplied to the water preparation module 200 ~~via~~by means of the cooling water return connection 2b and to the concentrate

mixing module 400 ~~via~~ by means of a mixing water feed connection 4a. One important role of the thermal control and ~~sterilisation~~sterilization module 300 is to prevent heat being wasted and to sequence heating operations, so that the apparatus does not require more power than can be supplied by a domestic electricity socket. The apparatus 100 is designed to operate with a mains electricity supply of either 90-140V, 10A, 50/60 Hz (for example in North America and Japan) or 198-253V, 10A, 50/60 Hz (for example in Europe). The maximum power consumption of the apparatus 100 is therefore between 0.9 kW and 2.5 kW. During filling of the patient with PD fluid, the power consumption is around 1.2 kW. If the electricity supply is unable to provide sufficient power to ~~sterilise~~sterilize the PD fluid at a flow rate of 300 ml/min, the flow rate is reduced, for example to 150 ml/min, to reduce the power required to ~~sterilise~~sterilize the PD fluid. The major part of the energy consumption of the apparatus 100 is required for heating of water and PD fluid for disinfection and ~~sterilisation~~sterilization during filling of the patient.

[0209] The connections between the water preparation module 200 and the thermal control and ~~sterilisation~~sterilization module 300 are described above. The thermal control and ~~sterilisation~~sterilization module 300 also supplies temperature controlled purified water to the concentrate mixing module 400 via the mixing water feed connection 4a. The output, for example PD fluid, of the concentrate mixing module 400 is returned to the thermal control and ~~sterilisation~~sterilization module 300 ~~via~~ by means of a mixing module output connection 4b.

[0210] The fluid entering the thermal control and ~~sterilisation~~sterilization module 300 at the mixing module output connection 4b passes through an input volumetric flow meter 350 which, when the apparatus is supplying PD fluid to the patient, measures the volume of fluid supplied to the patient. An output volumetric flow meter 650 is provided in the cyclor and ~~sterilisable~~sterilizable connector module 600

and measures the volume of fluid removed from the patient. The change in the patient's body fluid level due to the PD treatment is calculated by subtracting the volume of fluid drained from the patient from the volume of fluid supplied to the patient. This change is called the ultrafiltration volume (UF) and is measured in the range -4 litres to +10 litres over the treatment session to an accuracy of ± 66 ml (or 0.66% of the total fill volume, if greater), preferably ± 33 ml (or 0.33% of the total fill volume, if greater).

[0211] When treating the patient, sterile PD fluid is passed from the thermal control and ~~sterilisation~~ sterilization module 300 to the cyclor and ~~sterilisablesterilizable~~ connector module 600 via a sterile fluid connection 8a. During ~~sterilisation~~ sterilization of the cyclor and ~~sterilisablesterilizable~~ connector module 600, water at ~~sterilisation~~ sterilization temperature is passed from the thermal control and ~~sterilisation~~ sterilization module 300 to the cyclor and ~~sterilisablesterilizable~~ connector module 600 ~~via~~ by means of the sterile fluid connection 8a and returned to the thermal control and ~~sterilisation~~ sterilization module 300 ~~via~~ by means of a ~~sterilisation~~ sterilization output connection 8b. The ~~sterilisation~~ sterilization water is returned to the cyclor and ~~sterilisablesterilizable~~ connector module 600 after heat recovery by the thermal control and ~~sterilisation~~ sterilization module 300 ~~via~~ by means of a ~~sterilisation~~ sterilization fluid return connection 8c.

[0212] The thermal control and ~~sterilisation~~ sterilization module 300 connects to the drainage module 500 ~~via~~ by means of a thermal drain connection 13a, which is used to pass the waste water from the purification waste connection 2d to the drainage module 500 after heat recovery. During disinfection, fluid is passed at low pressure from the drainage module 500 to the thermal control and ~~sterilisation~~ sterilization module 300 for heat recovery ~~via~~ by means of a heat recovery drain connection 13b. This fluid is returned to the drainage module

500 after heat recovery ~~via-by means of~~ a heat recovery drain return connection 13c.

[0213] The concentrate mixing module 400 mixes concentrated PD fluid to the required recipe and supplies the PD fluid, suitably diluted, to the thermal control and ~~sterilisation~~ sterilization module 300 for ~~sterilisation~~ sterilization. The concentrate mixing module 400 also supplies cleaning agent to downstream modules of the apparatus, and controls the venting of air from the fluid circuit, while keeping microbiological contamination to a minimum.

[0214] As explained above, purified water is supplied to the concentrate mixing module 400 ~~via-by means of~~ the mixing water feed connection 4a from the thermal control and ~~sterilisation~~ sterilization module 300, and chemically controlled PD fluid is returned to the thermal control and ~~sterilisation~~ sterilization module 300 via the mixing module output connection 4b. The concentrate mixing module 400 also has an air vent connection 6 to atmosphere to allow filling and draining of the fluid system, and a mixing module drain connection 15, which is used to supply water at disinfection temperature to the drainage module 500. Water at disinfection temperature is also supplied to the water preparation module 200 ~~via-by means of~~ the RO membrane disinfection connection 3.

[0215] The PD fluid is prepared by the concentrate mixing module 400 from concentrated components of the PD fluid provided in a disposable concentrate container 402 which connects to a manifold 404 of the concentrate mixing module 400 and is enclosed by a manifold cap 406.

[0216] Turning now to the drainage module 500, this module controls the flow of fluid to the external waste connection 16 and provides the negative pressure required to drain the patient of dialysate (the fluid removed from the patient at the end of a PD treatment). The external waste connection 16 may be permanently connected to the domestic sewerage system or temporarily connected, for example clipped over a lavatory bowl. The drainage module 500 also closes the drain line to

isolate the fluid system when necessary, and stops the flow from the water preparation module to allow disinfection. The maximum flow rate to the external waste connection 16 is 3 litres/min and the maximum temperature of the fluid passing through the external waste connection 16 is 85°C.

[0217] The majority of the connections to the drainage module 500 have been described in relation to the other modules of the apparatus. The remaining connections, to the cyclor and ~~sterilisable~~sterilizable connector module 600, will be described below.

[0218] The cyclor and ~~sterilisable~~sterilizable connector module 600 prevents PD fluid of unsafe chemical composition, temperature or pressure or non-sterile PD fluid from being passed to the patient 50, by closing off the appropriate supply lines. As described above, the cyclor and ~~sterilisable~~sterilizable connector module 600 is connected to the thermal control and ~~sterilisation~~sterilization module 300 ~~via—by means of the sterile fluid connection 8a, the ~~sterilisation~~sterilization output connection 8b and the ~~sterilisation—sterilization fluid return connection 8c.~~ The cyclor and ~~sterilisable~~sterilizable connector module 600 connects to the patient 50 ~~via—by means of a patient fill connection 9a and a patient drain connection 9b.~~ The patient connections, 9a, and 9b, are made to a disposable fluid line 10 which is replaced by the patient 50 at the start of each PD treatment session and connects to the standard connector on the catheter (not shown) into the patient's peritoneal cavity. The disposable fluid line 10 is provided to the patient ~~pre-sterilise~~sterilized and in a sterile package. The disposable fluid line 10, which may be seen in Fig. 19, 20 and 21, has a pierceable membrane 634 at the end that connects to the cyclor and ~~sterilisable~~sterilizable connector module 600 and this membrane 634, in combination with a cap (not shown) on the catheter connector 654, maintains the sterility of the disposable fluid line 10 until it is used.~~

[0219] The cyclor and ~~sterilisable~~sterilizable connector

module 600 is arranged such that the fluid circuit from the sterile fluid connection 8a to the ~~sterilisation~~-sterilization output connection 8b which includes the pierceable membrane 634 at the end of the disposable fluid line 10 can be heat ~~sterilise~~sterilized with water at ~~sterilisation~~-sterilization temperature from the thermal control and ~~sterilisation~~ sterilization module 300. The cyclor and ~~sterilisable~~sterilizable connector module 600 maintains the sterility of the fluid circuit once the membrane 634 on the fluid line 10 has been pierced until the end of the treatment session, and also ensures that fluid can only be passed to the patient when intended.

[0220] The cyclor and ~~sterilisable~~sterilizable connector module 600 has a negative pressure drain connection 14a to the drainage module 500 for draining the dialysate from the peritoneal cavity of the patient, and an ambient pressure drain connection 14b which is used to drain fluids other than the dialysate from the cyclor and ~~sterilisable~~sterilizable connector module 600.

[0221] The sampling module 700 is connected to the disposable fluid line 10 via sampling interface 11 and collects a 15 ml sample of dialysate, when requested, for analysis. The sample represents an average of the composition of the drained dialysate over all the cycles of the treatment session.

[0222] The structure of the individual modules will now be described in more detail with reference to the figures.

[0223] Water Preparation Module 200

[0224] Figure 3 shows in detail the structure of the water preparation module 200. Tap water from the domestic mains supply enters the water preparation module 200 through the tap water connection 1. The flow of mains water can be switched off completely by an inlet valve 202. From the inlet valve 202, the water passes through a 30 micron particulate filter 204 which protects the moving parts of the water preparation module 200 from coarse particles in the water supply. The

filter 204 also prevents damage or blocking of the downstream components of water preparation module 200, such as reverse osmosis membranes or particle filters.

[0225] The filtered water passes through a water softener 206, for example in the form of an ion exchange column. Waste water from the water softener 206 produced during regeneration of the water softener 206 is passed to the drainage module 500 via-by means of a normally closed water softener valve 268, the purification waste connection 2d and the thermal drain connection 13a of the thermal control and ~~sterilisation~~sterilization module 300. The water softener 206 protects the fluid components of the water preparation module 200, such as reverse osmosis (RO) membranes, 238, and 252, from lime scale which would degrade their performance. It is important for the operation of the RO membranes, 238, and 252, that the supplied water is soft in order to prevent a build-up of lime scale.

[0226] The softened water passes to an isolator 208, in the form of a tank equipped with a float valve, which prevents a back flow of material from the water preparation module 200 into the mains supply and also reduces the pressure of the water from mains pressure to atmospheric pressure. Air from the isolator 208 is directed to atmosphere at the isolator air vent 17, which can be opened and closed by an isolator air vent valve 209. The isolator 208 is also able to receive air from and pass air to the thermal control and ~~sterilisation~~sterilization module 300 via-by means of the patient heat exchanger vent connection 2e.

[0227] Downstream of the isolator 208, a branch of the fluid path including the disinfection cartridge 210 connects to the main fluid path and will be described later. The softened water in the main fluid path passes from the isolator 208 to the thermal control and ~~sterilisation~~sterilization module 300 via-by means of the cooling water output 2a and is used in the thermal control and ~~sterilisation~~sterilization module 300 for cooling purposes and pre-heating before being

returned to the water preparation module 200 via-by means of the cooling water return connection 2b at a controlled temperature of approximately 30°C. The raised temperature of the water due to the preheating in the thermal control and ~~sterilisation~~sterilization module 300 reduces the power required to pump the water through the RO membranes and improves the effectiveness of the degassing operation described below.

[0228] The preheated water returning to the water preparation module 200, via-by means of the cooling water return connection 2b passes through a series of components, 214- through 224, which remove dissolved gas from the water. These components are a proportioning valve 214, a degassing restrictor 216, an expansion chamber 218, a degassing pump 222 and a degassing chamber 224. In operation, water from the degassing chamber 224 is recirculated via-by means of the proportioning valve 214 through the degassing restrictor 216 by the degassing pump 222, which is a gear pump. The pressure drop in the water due to the degassing restrictor 216 causes dissolved gas in the water to be forced out of solution and begin to form bubbles in the water. The pressure drop due to the degassing restrictor 216 is a function of the flow rate there through, which is maintained constant by recirculation from the degassing chamber 224, at a flow rate set by the degassing pump 222.

[0229] The degassing chamber 224 includes a level sensor 225, such as an ultrasonic level sensor, which detects the level of the water in the degassing chamber 224. The level sensor 225 controls the operation of the proportioning valve 214 such that if the level of water in the degassing chamber 224 drops, the proportioning valve 214 is adjusted to allow water from the cooling water return connection 2b to supplement the water recirculated by the degassing pump 222 until the water level in the degassing chamber 224 returns to the maximum level. The recirculated flow from the degassing chamber 224 is decreased to maintain the flow through the

degassing restrictor 216 constant. In this way, any flow of water out of the degassing chamber 224 downstream towards the RO membranes 238,252 is replaced by a flow of water at the same rate from the cooling water return connection 2b. However, the flow rate through the degassing restrictor 216 remains constant regardless of the downstream flow rate from the degassing chamber 224 due to the operation of the proportioning valve 214. A constant flow of 900 ml/min through the degassing restrictor 216 gives a pressure drop of 800 mbar (80 kPa), which is sufficient for effective degassing.

[0230] The reduced pressure water passes from the degassing restrictor 216 to the expansion chamber 218 which slows the flow sufficiently that bubbles of gas initiated during the rapid pressure reduction in the restrictor combine and have time to increase in size. Some of the bubbles rise to the surface of the water in the expansion chamber 218 and form a small head space of gas in the expansion chamber 218. The expansion chamber is provided with a gas-pipe 219 which connects the headspace in the expansion chamber 218 to the fluid path between the expansion chamber 218 and the degassing pump 222, so that gas bubbles are entrained in the fluid drawn from the expansion chamber 218 by the degassing pump 222. The mixture of gas and water are drawn from the expansion chamber 218 by the degassing pump 222 and the pressure of the water is monitored by a degassing pressure sensor 220 to ensure that the pressure is sufficiently low for effective degassing. The degassing pump 222 pumps the gas and water into the degassing chamber 224 where the gas is vented to the isolator 208 at atmospheric pressure. The level sensor 225 in the degassing chamber 224 controls the fluid flow through the proportioning valve 214 as described above by opening the proportioning valve 214 to increase the proportion of the flow through the degassing restrictor 216 directly from the cooling water return connection 2b when the water level drops due to water being drawn from the degassing chamber 224 by downstream components of the water preparation module 200. In this way,

fluid continuity in the subsequent sections of the water preparation module 200 is ensured.

[0231] A bypass from upstream of the proportioning valve 214 directly to the degassing pressure sensor 220 under the control of a degassing bypass valve 226 is provided so that disinfection can take place without the pressure drop associated with the degassing restrictor 216.

[0232] The degassed water from the degassing chamber 224 is drawn by an RO pump 236 (Model Procon 1608, from Procon Products Div./Roehlen Industries, Ten, USA) through an incoming water conductivity meter 228 which, in combination with an incoming water temperature sensor 230, measures the conductivity of the water. Each conductivity measurement of the water (or the PD fluid) by the apparatus 100 of the invention is accompanied by a temperature measurement, as the measured conductivity of a solution varies with temperature. The conductivity measurements are compensated by reference to the temperature at which they are taken to provide an indication of the ionic concentration in the water (or PD fluid).

[0233] After the conductivity measurement, the water passes through an activated carbon filter 232, available from Gambro AB of Lund, Sweden as part No. K06735001, the purpose of which is to remove free chlorine from the water and to adsorb some organic contaminants. Chlorine in the water can damage the surface of the membranes of the RO membrane units, 238, and 252.

[0234] Following the activated carbon filter 232 the water passes through a 5 micron particulate filter 234 which removes from the water any traces of carbon or other particulate matter not caught by the first filter 204 which could foul the RO membranes in units, 238-252.

[0235] The filtered water is pumped by the high pressure RO pump 236, preferably a rotary vane pump, past the surface of a first membrane in a RO membrane unit 238 (Type HSRO/2521/FF from Dow Film Tech, USA) and through a first RO output

restrictor 240 to the drainage module 500 via-by means of the purification waste connection 2d and the thermal control and sterilisationsterilization module 300. The high pressure of the water passing over the surface of the membrane in the first RO membrane unit 238 causes some of the water to pass through the membrane in RO membrane unit 238 overcoming the osmotic counterpressure caused by the ions in the retained liquid, in a reverse osmosis process. The remaining water, which includes any impurities which were present in the water, passes through the first RO output restrictor 240 to the purification waste connection 2d. The first RO output restrictor 240 maintains the pressure across the first membrane in RO membrane unit 238 to ensure effective reverse osmosis.

[0236] A first RO differential pressure sensor 242 is provided to measure the differential pressure between the inflow to the first RO membrane unit 238 and the waste flow therefrom (before the first RO output restrictor 240), in order to detect fouling of the first RO membrane unit 238. If the membrane in RO membrane unit 238 begins to foul, the resistance of the membrane to the tangential flow between inlet and waste begins to increase. Due to the largely constant flow that is delivered from the RO pump, the pressure differential is increased. When the pressure differential increases by greater than say 0.5 Bar, which is sensed by a differential pressure sensor, 242a and 242b, the membrane is considered fouled. If the membrane in the RO membrane unit 238 begins to foul, there is also a higher pressure drop across the membrane, which is sensed by pressure sensors 242a and 242c.

[0237] The first RO differential pressure sensor 242 is in the form of two cavities separated by a diaphragm with one cavity in fluid communication with a point before the first RO membrane unit 238, as indicated by circle 242a, and one cavity in fluid communication with a point on the waste water output of the first RO membrane unit 238 before the first RO output

restrictor 240, as indicated by circle 242b, or after the membrane in RO membrane unit 238, as indicated by circle 242c. The differential pressure is measured by monitoring the deformation of the diaphragm towards one or the other cavity. It is not necessary for the control system to measure the absolute pressure at the locations of the first RO differential pressure sensor 242a, as only the differential pressure is required to detect fouling of the first RO membrane in RO membrane unit 238.

[0238] The conductivity of the RO water which has passed through the first membrane in RO membrane unit 238 is measured by a first RO conductivity meter 246 in combination with a first RO water temperature sensor 248.

[0239] A first RO membrane bypass valve 250 is provided for use in the disinfection of the water preparation module 200, and its function will be described below.

[0240] A second RO membrane unit 252 (Type HSRO/2521/FF from Dow Film Tech, USA) is provided downstream of the first RO membrane unit 238. The use of two RO membrane units, 238, and 252, gives a much higher purity of water than would be the case with only one membrane unit and also gives additional security in the event that one membrane ruptures. When measured in terms of conductivity, the first RO membrane unit 238 filters out approximately 98% of impurities from the water pumped across it by the RO pump 236, and the second RO membrane unit 252 filters out 80% of the remaining 2% of impurities. The quality of water required by the apparatus 100 is very high and may be difficult to achieve consistently with a single RO membrane. If one of the RO membranes, 238, and 252, ruptures, the other membrane will continue to provide purified water for the short period of time before the fault is detected by the protective system and the apparatus 100 is stopped.

[0241] The waste water from the second RO membrane unit 252 passes through a second RO output restrictor 254 in the same way as for the first RO membrane unit 238, except that this

waste water is recycled through a disinfectant selection valve 256 back to the input of the RO pump 236. This is possible because the waste water from the second RO membrane unit 252 is already reasonably pure as it has passed through the first RO membrane unit 238. This recycling improves the overall water usage efficiency of the apparatus. Typically, in operation of the apparatus a flow rate of 750 ml/min of water is drawn from the degassing chamber 224 by the RO pump 236. This flow rate is supplemented by 250 ml/min of water recycled from the second RO membrane unit 252, so that 1000 ml/min of water is pumped towards the first RO membrane unit 238. Of this 1000 ml/min of water, 500 ml/min passes to the purification waste connection 2d and 500 ml/min of purified water passes through the first RO membrane unit 238 to the second RO membrane unit 252. At the second RO membrane unit 252, a flow of 250 ml/min of water passes through the membrane to the purified water connection 2c and a flow of 250 ml/min is recycled back to the input of the first RO membrane unit 238.

[0242] A second RO differential pressure sensor 258 is provided to measure the differential pressure between the inflow and the waste flow of the second RO membrane unit 252 to detect fouling. The operation is the same as described in connection with the first RO differential pressure sensor 242, and the second RO differential pressure sensor 258 is divided in two cavities, a first cavity 258a and a second cavity 258b or 258c.

[0243] A RO pressure relief valve 260 is provided between the inflow to the second RO membrane unit 252 and the waste outflow therefrom, in order to control the pressure of the water presented to the second RO membrane unit 252, and to avoid a pressure build-up as the output demand at the purified water connection 2c varies. It is noted that the output demand from the second RO membrane unit 252 varies from full output, for example 250 ml/min, to zero during certain periods and anything there between. If the output from the second RO

membrane unit 252 becomes small or zero, relief valve 260 shunts water in parallel to the restrictor 254 to thereby maintain approximately the same operation conditions for the first RO membrane unit 238 as with full output. This operation also reduced water consumption.

[0244] A second RO conductivity meter 262 and a second RO temperature sensor 264 are provided at the output of the second RO membrane unit 252 to measure the conductivity of the output water, in order to ensure that the water has been sufficiently purified from ionic components. An output water pressure sensor 266 is provided downstream of the second RO temperature sensor 264 to measure the pressure of the water output via the purified water connection 2c to the thermal control and ~~sterilisation~~sterilization module 300.

[0245] During disinfection of the water preparation module 200, the disinfectant selection valve 256 is opened to direct the waste flow from the second RO membrane unit 252 through the disinfection cartridge 210. The disinfection cartridge 210 contains a chemical disinfectant, such as an aqueous solution of peracetic acid (a widely approved disinfectant), which is diluted by the water flow. During disinfection, a disinfection valve 212 is opened, the mains valve 202 is closed and flow through the purification waste connection 2d is prevented by the drainage module 500. The float valve of the isolator 208 prevents any backflow through the water softener 206. The first RO membrane bypass valve 250 is opened so that the waste water from the first RO membrane unit 238 is returned to the output side of the first RO membrane unit 238 rather than passing to the drainage module 500 ~~via~~by means of the purification waste connection 2d, which is closed by the drainage module 500. Degassing bypass valve 226 is opened to allow fluid flow there through. It will be seen therefore that a closed recirculation loop is created for circulation of the chemical disinfectant through the water preparation module 200. This closed loop disinfects most of the components and fluid paths of the water preparation module 200. However, to

disinfect the fluid path between the disinfectant selection valve 256 and the RO pump 236, the disinfectant selection valve 256 is closed so that disinfection fluid already in the fluid channel between the second RO restrictor 254 and the disinfectant selection valve 256 is circulated past the disinfectant selection valve 256 and through the RO pump 236.

[0246] A further recirculation path is provided from the gas output of the degassing chamber 224 through the isolator 208 and the degassing bypass valve 226, so that disinfection fluid is able to circulate through the isolator 208. The degassing bypass valve 226 is opened to allow fluid flow there through, so that the pressure of the disinfection fluid is not reduced by the degassing restrictor 216, which could cause the peracetic acid to form hydrogen peroxide, thereby reducing its effectiveness. Likewise, in the case of hot water disinfection, the drop in pressure through the degassing restrictor 216 could cause the water to boil. Although the degassing bypass valve 226 is opened, a small portion of the disinfection fluid is still passed through the degassing restrictor 216 to disinfect this fluid path.

[0247] Once all components downstream of the water softener 206 have been disinfected, the disinfection fluid is passed to the drainage module 500 through the purification waste connection 2d.

[0248] Water at disinfection temperature is introduced into the output side of the second RO membrane unit 252 via-by means of the RO membrane disinfection connection 3 for disinfection of the components of the water preparation module downstream of the second RO membrane unit 252.

[0249] In the case of heat disinfection of the water preparation module 200, the disinfectant cartridge 210 is not required and the water is heated during disinfection by the thermal control and ~~sterilisation~~sterilization module 200 between the cooling water output 2a and the cooling water return connection 2b.

[0250] Thermal Control and ~~Sterilisation~~Sterilization

Module 300

[0251] Figure 4 shows in detail the structure of the thermal control and ~~sterilisation~~sterilization module 300. Water from the cooling water output 2a of the water preparation module 200 is directed through a purification waste heat exchanger 324, where it is preheated by the water from the purification waste connection 2d passing through the purification waste heat exchanger 324 to the thermal drain connection 13a. The water heated by the purification waste heat exchanger 324 is heated by an electric water heater 322 before exiting the cooling water return connection 2b to ensure that it is at the optimum operating temperature for the water preparation module 200, normally about 30°C.

[0252] In the thermal control and ~~sterilisation~~sterilization module 300, water is circulated, in normal operation, by a patient output heat exchanger pump 316, in the form of a gear pump through a patient output heat exchanger 314 and a recirculation restrictor 310. The patient output heat exchanger 314 is in the form of a bath of water through which the fluid from an online autoclave 375 (described later) passes in a sealed conduit. The bath is kept at a constant temperature by the recirculating water to maintain the PD fluid passed to the patient at the required delivery temperature. If the temperature of the recirculating water is too high, a patient output heat exchanger drain valve 318 is opened so that the heated water can pass out of the patient output heat exchanger 314 to the cooling water return connection 2b via a patient output heat exchanger drain restrictor 308 and the water heater 322. A corresponding amount of colder water is drawn from the cooling water output 2a of the water preparation module 200 by the patient output heat exchanger pump 316, until the temperature of the heating bath of the patient output heat exchanger 314 has been reduced to the desired level

[0253] When it is not desired to extract heat from the patient output, for example because the patient output fluid

lines are being ~~sterilise~~sterilized at high temperature, the patient output heat exchanger 314 is drained under the influence of gravity by opening the patient output heat exchanger drain valve 318 and an air bleed valve 320. Air enters the patient output heat exchanger 314 through the patient output heat exchanger vent connection 2e from the isolator 208 via the opened air bleed valve 320 and an air bleed restrictor 312. When the patient output heat exchanger 314 is full of air, rather than water, negligible heat is transferred to or from the patient output fluid. In this case, the patient output heat exchanger pump 316 is inactive. The patient output heat exchanger 314 is refilled by opening the air bleed valve 320 to vent the air and reactivating the patient output heat exchanger pump 316 with the patient output heat exchanger drain valve 318 closed.

[0254] The purified water produced by the water preparation module 200 is passed to the thermal control and ~~sterilisation~~sterilization module 300 via the purified water connection 2c. The purified water passes through a disinfection heat exchanger 326 which is used during disinfection of the concentrate mixing module 400 to preheat the purified water by recovering heat passing from the heat recovery drain connection 13b to the heat recovery drain return connection 13c. The preheated water exiting the disinfection heat exchanger 326 is heated to disinfection temperature by an electric disinfection heater 330. During normal operation of the apparatus, the disinfection heater 330 is used to control the temperature of the water exiting the mixing water feed connection 4a to the concentrate mixing module 400.

[0255] During disinfection of the drainage module 500, water from the purified water connection 2c bypasses the disinfection heat exchanger 326 ~~via~~by means of a disinfection heat exchanger bypass valve 328, so that the water exiting the heat recovery drain return connection 13c remains at the disinfection temperature of about 85°C. The disinfection heat

exchanger bypass valve 328 is only used during disinfection of the drainage module 500.

[0256] The PD fluid produced by the concentrate mixing module 400 is passed to the thermal control and ~~sterilisation~~sterilization module 300 via ~~by means of~~ the mixing module output connection 4b. This fluid passes through the input volumetric flow meter 350 which records the flow of PD fluid filled into the patient. The PD fluid is drawn by a gear-type, volumetric pump 352 which is monitored by a tachometer 354 to ensure that the pump is operating at the expected volume flow rate. The delivery rate of the volumetric pump 352 is also monitored independently by the input volumetric flow meter 350 to ensure correct operation. The volumetric pump 352 delivers the PD fluid at the required rate and pressure for on-line autoclaving, i.e. 300 ml/min and 6 bar absolute (600 kPa) to prevent the fluid from boiling at 150°C. A gear type pump has been selected to ensure that the water passing through the online autoclave 375 can be pressurised by the pump to the pressure necessary for the water to be heated to ~~sterilisation~~sterilization temperature.

[0257] In normal operation of the apparatus 100, the PD fluid passes into the on-line autoclave (OLA) 375 through an OLA input valve 356. At this point, the pressure of the PD fluid is monitored by two independent OLA pressure sensors 358. One of the OLA pressure sensors 358 provides a pressure reading to the control system for the apparatus, the other sensor provides a reading to the separate protective system, see Figure 1a, which ensures that, even in the event of the apparatus malfunctioning, patient safety is not compromised. The pressure, temperature and conductivity sensors which are positioned to monitor parameters that are crucial to the patient's safety in the system are all duplicated in this manner, so that the patient is never endangered by a single sensor malfunction and each patient safety measurement is independently double-checked.

[0258] Downstream of the OLA pressure sensors 358 the PD

fluid passes through a first OLA heat exchanger 360 and a second OLA heat exchanger 362, both of which preheat the PD fluid entering the OLA heating bath 364 by recovering heat from the fluid exiting the OLA heating bath 364. The OLA heating bath 364 is an oil heating bath heated by an electric heater 365 and provided with a recirculation pump 366 (gear pump) and a heating bath temperature sensor 368. The oil or ethylene glycol is circulated by the recirculation pump 366 through a heating fluid path 367 which includes the oil bath and the PD fluid (or water) passes through a ~~sterilisation~~sterilization fluid path 369. The heating fluid path 367 and the ~~sterilisation~~sterilization fluid path 369 are separated by a thermally conductive barrier.

[0259] In order to ensure that the liquid leaving the OLA heating bath 364 is sterile, a parameter is defined which represents a ~~sterilising~~sterilizing~~sterilizing~~ value for the ~~sterilisation~~sterilization process and which can be calculated, for example, from an algorithm modelling the temperature distribution inside the OLA heating bath 364, and from the value of at least one other parameter which influences the ~~sterilisation~~sterilization treatment, namely the flow rate Q of the liquid to be ~~sterilise~~sterilized in the OLA heating bath 364, the temperature (T_{in}) of the liquid to be ~~sterilise~~sterilized entering the OLA heating bath 364 and the temperature (T_{Hin}) of the heating liquid (ethylene glycol) entering the OLA heating bath 364. Since the temperatures at the outlet of the OLA heating bath 364 (temperature of the ~~sterilise~~sterilized liquid and temperature of the heating liquid) are linked to the temperatures at the inlet of the OLA heating bath 364, it is also possible to take into account in the calculations the temperature (T_{out}) of the ~~sterilise~~sterilized liquid leaving the OLA heating bath 364 and/or the temperature (T_{Hout}) of the heating liquid leaving the OLA heating bath 364.

[0260] When the parameter representing the ~~sterilising~~sterilizing~~sterilizing~~ value for the treatment is

defined, a set value for this parameter is then chosen which is both high enough to correspond to an effective ~~sterilisation~~sterilization of the liquid, and as low as possible in order to prevent or limit the degradation of the liquid to be ~~sterilise~~sterilized when this liquid is heat-sensitive (as in the case of solutions for peritoneal dialysis which contain glucose).

[0261] During functioning, the control system of the apparatus 100 is programmed to calculate, at regular intervals, the value of the parameter representing the ~~sterilising~~sterilizing value for the treatment, from the algorithm of temperature distribution in the OLA heating bath 364, and the temperature and flow rate data measured by the OLA temperature sensors 370, the heating bath temperature sensor 368 and the input volumetric ~~flowmeter~~flow meter 350. Each time that a new value for the parameter is calculated, the control system checks that this calculated value is higher than the set value and therefore confirms that the liquid is sterile. A further temperature sensor 379 is used for obtaining the temperature of the liquid to be ~~sterilise~~sterilized by the OLA before entering the heat exchanger.

[0262] This checking process, which allows validation of the effective ~~sterilisation~~sterilization of the liquid, can be passive. The reason for this is that, given that the sterile state is a crucial characteristic of the PD fluid it is possible to envisage a standard operating mode for the OLA 375 in which the choice of the flow rate for the liquid to be ~~sterilise~~sterilized is limited to a restricted number of different predetermined values (for example three) and in which all of the other operating parameters for the device are preset as a function of the predetermined flow rates, such that the functioning of the device is simplified as much as possible. In this case, the checking process described above is used merely to validate the ~~sterilisation~~sterilization.

[0263] It is also possible to envisage an operating mode

for the OLA 375 in which the choice of flow rate of liquid to be ~~sterilise~~sterilized is free within a range of determined values. In this case, the control system calculates, from the chosen flow rate and from the set value for the parameter representing the ~~sterilising~~sterilizingsterilizing value, the other operating parameters for the device, in particular the temperature of the heating liquid as measured by temperature sensor 368. During functioning, the control system regularly adjusts the flow rate of the volumetric pump 352 and/or the temperature of the heating liquid circulated by the recirculation pump 366, such that the calculated value of the parameter is always greater than the set value.

[0264] The parameter denoted in the literature (see page 288 of the European Pharmacopoeia 1997, or page 1977 of the United States Pharmacopoeia, 23rd Edition) as F_0 (expressed in minutes) is used as the parameter representing the ~~sterilising~~sterilizingsterilizing value for the ~~sterilisation~~sterilization process. F_0 is the sum of the cumulative ~~sterilising~~sterilizingsterilizing effects during a ~~sterilisation~~sterilization treatment, or ~~sterilising~~sterilizingsterilizing value F_T^Z when the reference temperature T is equal to 250°F (121.1°C) and the thermal inactivation value Z is equal to 18°F (10°C). The thermal inactivation value Z is the temperature increase which multiplies by ten the rate of destruction of a specific microorganism. $Z = 10^\circ\text{C}$ corresponds to a theoretical microorganism which is slightly more resistant than the microorganism reputed to be more heat-resistant than any other spore-forming microorganism, *Bacillus stearothermophilus*. The canonical formula for F_0 is shown in Equation 1.

$$F_0 = \int_0^t \left(\frac{T - 121}{10} \right) dt \quad (1)$$

[0265] This formula cannot be applied directly to the checking of a ~~sterilisation~~sterilization treatment in which the liquid to be ~~sterilise~~sterilized is permanently flowing

and in which the heating means used to raise the temperature of the liquid to be ~~sterilise~~sterilized does not bring this liquid to the same temperature at all points in the heating chamber.

[0266] When the heating means is arranged to heat the liquid to be ~~sterilise~~sterilized along a portion of the pipe in which the liquid is circulating, it is the believed that the formula shown in Equation 2 can be used to calculate F_0 .

$$F_0 = \int_0^L \frac{S}{Q} \times 10^{\left(\frac{T(y)-121}{10}\right)} dy \quad (2)$$

In equation 2:

L = length of the ~~sterilisation~~sterilization fluid path 369 of the liquid to be ~~sterilise~~sterilized through the OLA heating bath 364;

S = internal cross section of the ~~sterilisation~~sterilization fluid path 369 through the OLA heating bath 364;

Q = flow rate of the liquid to be ~~sterilise~~sterilized through the OLA heating bath 364;

T(y) = equation of the temperature distribution of the liquid as a function of the distance from the inlet of the OLA heating bath 364.

[0267] The equation T(y) depends on the structure of the OLA heating bath 364 and on its operating mode. For example, Figure 8 shows a first example of a heat exchanger which is adapted for use in the OLA 375. This exchanger consists of two concentric pipes, the outer pipe forming a sleeve around the inner pipe. The ~~sterilisation~~sterilization fluid path 369 is provided by the interior of the inner pipe and the heating fluid path 367 is provided between the inner and outer pipe.

[0268] During operation, the liquid to be ~~sterilise~~sterilized and the heating liquid, for example ethylene glycol, are circulated, in opposite directions, in the inner pipe (~~sterilisation~~sterilization fluid path 369) and in the outer pipe (heating fluid path 367). The inside diameter of the ~~sterilisation~~sterilization fluid path 369 is

chosen such that, in the range of flow rates which includes the flow rates for operating the OLA 375 (100 to 400 ml/min), the flow of the liquid to be ~~sterilise~~sterilized is always turbulent.

[0269] For an exchanger with an inner pipe made of stainless steel and an outer pipe made of copper and having the dimensions set out in Table 1 the equation for $T(y)$ can be written according to Equation 3.

Table 1

Length (cm)	222
Inner pipe volume (ml)	26
Outer pipe volume (ml)	105
Cross section of the inner pipe (cm ²)	0.117
Area of the annular space between the inner and outer pipes (cm ²)	0.502
Internal perimeter of the inner pipe (cm)	1.213
External perimeter of the inner pipe (cm)	1.995
Internal exchange area of the inner pipe (cm ²)	269
External exchange area of the inner pipe (cm ²)	443

$$T(y) = T_{in} + (T_{Hin} - T_{in}) \times \frac{rx[e^{-ny} - e^{-nL}]}{1 - rx e^{-nL}} \quad (3)$$

T_{in} = temperature of the liquid to be ~~sterilise~~sterilized entering the ~~sterilisation~~sterilization fluid path 369;

T_{Hin} = temperature of the heating liquid entering the heating fluid path 367 (such as measured by the heating bath temperature sensor 368).

$$r = 6 \times 10^{-3} \times Q^2 - 0.0577 Q + 19.084$$

$$n = -\frac{1}{L} \ln \left[\frac{301415 - 958.18Q + Q^2}{292.6 + 65.72Q - 0.200453Q^3 + 0.00020948} \right]$$

Q = flow rate of the liquid in the ~~sterilisation~~sterilization fluid path 369.

[0270] As emerges from this example, it is possible to calculate the ~~sterilising~~sterilizing value F_0 at any moment, from a measurement of the temperature T_{in} of the liquid

to be ~~sterilise~~sterilized entering the OLA heating bath 364, a measurement of the temperature T_{min} of the heating liquid entering the OLA heating bath 364, a measurement of the flow rate Q of liquid to be ~~sterilise~~sterilized and an equation modelling the temperature distribution inside the OLA heating bath 364.

[0271] In the preferred embodiment of the present invention, as shown in Figure 4, the OLA heating bath is in the form of a bath of ethylene glycol which is agitated by the recirculation of the ethylene glycol by the recirculation pump 366 to ensure a uniform temperature throughout the OLA heating bath 364. The ~~sterilisation~~sterilization fluid path 369 passes through the OLA heating bath 364 in a sealed conduit. The above principles are, however, applicable to the embodiment shown.

[0272] Throughout all the operating phases of the OLA 375 in which the OLA 375 is expected to produce a sterile liquid (water or PD fluid), the control system validates the ~~sterilisation~~sterilization treatment carried out by checking that the calculated ~~sterilising~~sterilizing value F_0 is always greater than a first threshold value F_{0min1} corresponding to the sterility of the liquid.

[0273] The OLA heating bath 364 heats the PD fluid to a temperature of greater than 150°C and maintains the PD fluid at this temperature for at least 2 seconds to autoclave the PD fluid and thereby ensure sterility. The flow rate through the OLA heating bath 364 is 300 ml/min. Under these conditions it is believed that the equivalent theoretical F_0 value is at least 20 minutes.

[0274] The temperature of the sterile PD fluid exiting the OLA heating bath 364 is checked by two independent OLA temperature sensors 370 which ensure that the required temperature has been reached. Most of the heat from the autoclaved PD fluid is recovered to the PD fluid entering the OLA heating bath by the first and second OLA heat exchangers 360, 362. Any residual heat is recovered in the patient output

heat exchanger 314 which ensures that the temperature is acceptable for the patient, i.e. 37°C. The temperature of the autoclaved PD fluid is checked downstream of the patient output heat exchanger 314 by two independent patient output temperature sensors 372. Finally, the pressure of the PD fluid is reduced by a patient output pressure relief valve 374 to a safe pressure for delivery to the patient. The autoclaved, pressure and temperature controlled PD fluid is then passed to the cyclor and ~~sterilisable~~sterilizable connector module 600 ~~via-by means of the~~ sterile fluid connection 8a.

[0275] During ~~sterilisation~~sterilization of the cyclor and ~~sterilisable~~sterilizable connector module 600 the fluid pumped by the volumetric pump 352 takes a different path through the OLA so that the fluid is at 130°C, rather than 37°C. The fluid is maintained at a pressure of 3 bar absolute (300 kPa) to prevent boiling. In this case, the fluid passes through an OLA ~~sterilisation~~sterilization valve 376 and through a ~~sterilisation~~sterilization heat exchanger 378 which recovers heat passing from the ~~sterilisation~~sterilization output connection 8b of the cyclor and ~~sterilisable~~sterilizable connector module 600 to the ~~sterilisation~~sterilization fluid return connection 8c. The heat recovered by the ~~sterilisation~~sterilization heat exchanger 378 is used to preheat the fluid, which then passes to the second OLA heat exchanger 362 for further preheating. The heating of the ~~sterilisation~~sterilization fluid by the OLA heating bath 364 is similar to the process for autoclaving the PD fluid. However, heat is only recovered by the second OLA heat exchanger 362 and not the first OLA heat exchanger 360 or the patient output heat exchanger 314. The patient output heat exchanger 314 has been drained at this stage so that it contains only air which is a poor conductor of heat and does not therefore transfer a significant amount of heat from the ~~sterilisation~~sterilization fluid. There is no flow through the heat-receiving side of the first OLA heat exchanger 360 because the OLA input valve 356 is closed and heat will not

therefore be transferred to the heat-receiving side of the first OLA heat exchanger 360 once the fluid in that side has reached the temperature of the fluid in the heat transferring side. Even though there is no flow, the fluid in the heat-receiving side of the first OLA heat exchanger 360 does not boil because it is in communication with the fluid flow through the OLA heating bath 364 and is therefore at the same pressure. Thus, the fluid for ~~sterilisation~~sterilization which exits the sterile fluid connection 8a has a much higher temperature, 130°C , than the fluid which is provided to the patient, and is therefore suitable for ~~sterilising~~sterilizing the cyclor and ~~sterilisable~~sterilizable connector module 600.

[0276] The ~~sterilisation~~sterilization of the cyclor and ~~sterilisable~~sterilizable connector module 600 is considered as effective when all of the points in the fluid circuit downstream of the OLA heating bath 364 have been brought, by means of the sterile liquid, to a minimum temperature T_2 for a minimum period t_2 , which corresponds to a second set ~~sterilising~~sterilizing value $F_{\text{omin}2}$, given by Equation 4

$$F_{\text{omin}2} = t_2 \times 10^{\left(\frac{T_2 - T_{21}}{10}\right)} \quad (4)$$

[0277] Validation of the ~~sterilisation~~sterilization of the fluid circuit can be achieved simply by the control system checking that, during an uninterrupted interval at least equal to t_2 , the temperature of the liquid measured by the patient output temperature sensors 372 has constantly been above T_2 .

[0278] Since the ~~sterilisation~~sterilization of the cyclor and ~~sterilisable~~sterilizable connector module 600 is to be carried out with sterile water, the control system must validate both the ~~sterilisation~~sterilization of the liquid and ~~sterilisation~~sterilization of the fluid circuit. In other words, the control system must check both that the ~~sterilising~~sterilizing value for the ~~sterilisation~~sterilization treatment applied to the liquid is greater than $F_{\text{omin}1}$ and that the ~~sterilising~~sterilizing value

for the ~~sterilisation~~sterilization treatment applied to the circuit is greater than F_{0min2} . For this reason, the second OLA heat exchanger 362 is used, as the temperature of the sterile liquid must be brought down from the fluid ~~sterilisation~~sterilization temperature of 150°C (necessary to achieve F_{0min1}) to the circuit ~~sterilisation~~sterilization temperature of 130°C (which is lower than 150°C so that the pressure required in the cyclor and ~~sterilisable~~sterilizable connector module 600 is only 3 bar absolute rather than 6 bar absolute).

[0279] The patient output pressure relief valve 374 operates during ~~sterilisation~~sterilization to maintain the fluid before the relief valve 374 at a high pressure of 6 bar absolute and the pressure after the relief valve at the high pressure of 3 bar absolute required to prevent boiling at 130°C . A skilled person realises how to construct such a valve. If the water began to boil, it would not be possible to validate the ~~sterilisation~~sterilization of the circuit, since it would not be possible to certify that every point of the circuit has come into contact with water at a minimum temperature for a minimum uninterrupted period of time.

[0280] The fluid path in the apparatus 100 is carefully insulated to prevent heat loss during disinfection and/or ~~sterilisation~~sterilization. In particular, the relative locations of the hot components are chosen to ensure that heat loss is kept to a minimum, i.e. adjacent components keep each other warm. In this way, it is ensured that the fluid paths are maintained at the correct disinfection or ~~sterilisation~~sterilization temperatures along the whole of the path. A temperature sensor 380 arranged at connection 8b may be used for verifying the sterility of the fluid circuit up to heat exchanger 378.

[0281] The heat exchangers 360, 362, 378 are in one embodiment shaped like the exchanger represented in Figure 9, i.e. with the junction on a part of their length of the heating pipe and the fluid pipe. The two portions of joined

pipes are shaped to form a coil with joined spirals, and both the inside and the outside of the cylinder thus formed are covered with a material which is a good heat conductor.

[0282] Other details of the thermal control and ~~sterilisation~~sterilization module 300 are described in our co-pending application entitled "Process and device for ~~sterilising~~sterilizing and dispensing a liquid for medical use", Gambro reference HP 1310, which is incorporated herein by reference and a copy of which is attached hereto.

[0283] Concentrate mixing module 400

[0284] Figure 5 shows in detail the structure of the concentrate mixing module 400. The concentrate mixing module 400 includes the disposable concentrate container 402 which interfaces with the manifold 404 and is covered by the manifold cap 406. The disposable concentrate container 402 includes chambers, in the form of compartments for an aqueous solution of lactic acid 408, cleaning agent 410 (for example powdered sodium carbonate), powdered sodium bicarbonate 412, powdered sodium chloride 414, powdered calcium chloride 416, powdered magnesium chloride 418 and powdered glucose 420. The disposable concentrate container 402 contains enough material in each compartment for a PD treatment session of the patient according to a selected one of a large number of prescriptions.

[0285] The range of composition for each of the components of the PD fluid which can be delivered to the patient stored in the disposable concentrate container 402 is set out in Table 2, together with the composition range for sodium lactate which is formed from the lactic acid and sodium bicarbonate. The mass of the components in the disposable concentrate container 402 and the approximate volume of each compartment 408-420 are also given in Table 2.

[0286] The concentration of sodium in the PD fluid delivered to the patient is within $\pm 2.5\%$ of the requested amount. The concentration of each of the other ingredients is within $\pm 5\%$ of the requested amount. This assumes a fill

volume of at least one ~~litre~~ liter. It is likely that for any given prescription, at least one of the components of the dialysis fluid in the container 402 will not be entirely used up, as the amounts are selected to cover a wide variety of prescriptions.

[0287] In addition or as an alternative to the components listed in Table 2, other components could be included, for example potassium salts.

Table 2

Component	Composition Range	Mass in compartment	Approx. volume of compartment
Sodium chloride	120-140 mmol/l	208g	300 ml
Magnesium chloride	0.25-0.50 mmol/l	36g	150 ml
Calcium chloride	1.0-2.0 mmol/l	52g	300 ml
Sodium lactate	0-40 mmol/l*	-	-
Sodium bicarbonate	0-40 mmol/l*	120g	150 ml
Lactic acid	Compatible with sodium lactate and sodium bicarbonate levels	120g	300 ml
Glucose	1.5-4.0% w/w	1176g	1800 ml
Sodium carbonate	-	20	150 ml
Note: *In any given solution, the molar concentrations of sodium lactate and sodium bicarbonate add up to between 30 and 40 mmol/l.			

[0288] It should be noted that the relative arrangement i.e. the order, of the compartments, 408- through 420, in Figure 5 (and Figure 5a) is schematic only, and does not represent any physical order, but is chosen to easily represent the topology of the fluid system. Figures 10 and 11 show the order of the compartments, 408- through 420, in the disposable concentrate container 402 according to one embodiment of the invention.

[0289] Figure 10 shows the construction of the disposable concentrate container 402. The compartments, 408- through 420,

are individually injection moulded in polypropylene and are mounted to a chassis 401 at their lower ends. The upper ends of the compartments, 408- through 420, are held together by a lid 403 which also serves to close off the upper end of the glucose compartment 420 and provide a carrying handle for the container 402. As is clear from Table 2, the lactic acid compartment 408, the sodium chloride compartment 414 and the calcium chloride compartment 416 are each approximately twice the volume of the cleaning agent compartment 410, the sodium bicarbonate compartment 412 or the magnesium chloride compartment 418. The glucose compartment 420 is significantly larger than the other compartments, 408- through 418. Each of the compartments, 408- through 418, is provided at its lower end with at least one connector 407 for connection to the manifold 404.

[0290] Figure 11 shows a partially sectional view through the disposable concentrate container 402 with part of the chassis 401 removed, and which clearly shows the connectors 407 of the compartments, 408- through 420. The glucose compartment 420 is provided with two connectors, 407a₇ and 407b, the function of which will be explained below.

[0291] Figures 12a to 12c show perspective views of the lid 403 (Figure 12a), glucose compartment 420 (Figure 12b) and chassis 401 (Figure 12c) of the disposable concentrate container. As shown in Figures 12a to 12c, the lower surface of the glucose compartment 420 is sloped to direct the glucose powder in the compartment 420 towards the input connector 407a. The connectors 407 of each of the compartments, 408- through 420, are received in corresponding holes 409 defined in the chassis 401. The holes 409 are aligned in the longitudinal direction of the chassis 401 along a line A which is offset by a distance from the longitudinal axis of symmetry B of the chassis 401. In this way, the container 402 is made rotationally asymmetric so that it cannot be inserted into the apparatus 100 the wrong way round.

[0292] The compartments, 408- through 418, are snapped in

place and the glucose compartment 420 is hot rivetted riveted (heat staked) to the chassis 401 using rivets 411 which are formed integrally with the compartment 420. The rivets 411 are received in corresponding holes 405 in the chassis 401. Also, the rivets 411 of compartments 408 to 418 may be hot rivetted riveted.

[0293] The chassis 401 includes a skirt 413 which is corrugated for strength and protects the connectors 407 when the container 402 is placed on a surface. The skirt or the connectors may be provided with a removable strip 443 for the protection of the connectors 407 during transport and storage.

[0294] Figure 13 shows the magnesium chloride compartment 418 as an example of the smaller size of compartments, 410, 412, and 418. Figure 14 shows the sodium chloride compartment 414 as an example of the larger size of compartments, 408, 414, and 416. The lower surface of each size of compartments, 410, 412, and 418, and 408, 414, and 416, slopes towards the connector 407 so that the powder (or liquid) in the compartments, 408- through 418, is directed towards the connector. Each compartments, 408- through 418, has a compartment lid 415 which is fitted to the compartments, 408- through 418, after the compartment has been filled with the respective powder or liquid. In this way, it is not necessary to fill the container, 408- through 418, through the narrow connector 407, which would be difficult. The compartment lids 415 are heat welded (hot melted) to the respective compartments, 408- through 418. As mentioned above, the container lid 403 also forms the lid which closes off the glucose compartment 420 and is heat welded thereto.

[0295] Referring back to Figure 5, a new disposable concentrate container 402 is connected to the manifold 404 at the beginning of a PD treatment session, after disinfection, and is disconnected and discarded once the treatment has finished. A connection motor 422 engages with the disposable concentrate container 402 and drives the container into connection with the manifold 404.

[0296] Functionally, the compartments, 408- through 420, of the disposable concentrate container 402 are of three types. The first type includes the lactic acid compartment 408, the cleaning agent compartment 410, the calcium chloride compartment 416 and the magnesium chloride compartment 418. This first type of compartment has an air vent channel 424 which extends from an upper region of the interior of the compartment to a direct opening to atmosphere in the manifold 404 when the compartments, 408, 410, 416, and 418, is connected to the manifold 404. The air vent channel 424 allows air to exit the compartments, 408, 410, 416, and 418, when water is introduced into the compartment via a fluid channel 426 of this type of container or when fluid is withdrawn from the compartment, 408, 410, 416, and 418, via by means of the fluid channel 426. The fluid channel 426 introduces the fluid in a lower region of the interior of the compartment, 408, 410, 416, and 418, so that the water contacts all of the material as the water level rises up the compartment.

[0297] This first type of compartment, 408, 410, 416, and 418, is used to contain powdered salts which are only required in small amounts, so that the salt can be included in an amount which dissolves completely without additional agitation when a sufficient amount of water is introduced into the compartment, or for salts which are already in a concentrated solution.

[0298] The second type of compartment, 412- and 414, is used for salts which are required in such large volumes that the compartment 412,414 would have to be too large to contain at once all of the water required to dissolve all of the required salt. Thus, compartment 412 contains sodium bicarbonate and compartment 414 contains sodium chloride. This type of compartment includes a combined air vent and fluid channel 428 and a combined priming and output channel 430. Initially the salt in this type of compartment, 412- and 414, is immersed (or primed) by introducing water through the combined priming and output channel 430 in a lower region of

the compartment, while air is vented from an upper region of the compartment through the combined air vent and fluid channel 428. The priming operation fills the compartment 412,414 with water to immerse all of the salt therein. A similar technique is described in EP-A-0278100-European Patent No. 278,100, which is incorporated herein by reference.

[0299] Once the salt has been fully wetted, water is drawn through the combined air vent and fluid channel 428 and allowed to percolate through and dissolve the salt, so that salt solution can be drawn off in a lower region of the compartment, 412_T and 414_T through the combined priming and output channel 430. As the salt solution is drawn from the compartment, 412_T and 414_T, the reduction in pressure causes a corresponding volume of water to enter the compartment, 412_T and 414_T, through the combined air vent and fluid channel 428 which is connected to a source of water.

[0300] It would be possible to operate the second type of compartment, 412_T and 414_T, in a similar manner to the first type of compartment, 408, 410, 416, and 418. For example, the compartment may be filled with water through the output channel 430 to dissolve the salt therein and the (substantially saturated) salt solution may be withdrawn through the output channel 430. Because the amount of salt in the second type of compartment, 412_T and 414_T, is larger than can be dissolved by the volume of water that fills the compartment, 412_T and 414_T, some salt will remain in the compartment, 412_T and 414_T, after the solution is withdrawn. The compartment, 412_T and 414_T, can therefore be refilled with water to obtain more solution.

[0301] The physical configuration of the first and second types of compartment is identical when the container 402 is not connected to the manifold 404. It is only the contents of the compartment and the arrangement of valves and air vents in the mixing module 400 which determines the type of the compartment.

[0302] The third type of compartment is the glucose

compartment 420. Glucose is particularly difficult to dissolve consistently and quickly in high concentrations, such as 50%, and therefore requires recirculation to ensure that all the glucose is dissolved. Furthermore, the volume of the glucose solution decreases as the glucose dissolves and thus the glucose compartment 420 requires continuous venting throughout the dissolution process. Thus, the glucose compartment 420 includes a glucose air vent channel 432 which is permanently connected to atmosphere when the disposable concentrate container 402 is connected to the manifold 404, a fluid input channel 434 which inputs water or recirculated glucose solution to a lower region of the glucose compartment 420, and a glucose output channel 436 which draws glucose solution from an upper region of the glucose compartment 420 through a glucose particle filter 438 which prevents particles of glucose from accidentally entering the fluid system.

[0303] The inventors have found that good results are achieved with monohydrate glucose, specifically LYCADEX PF/Dextrose mono pyrogen free from Roquette Freres S.A. of Lestrem, France, because this glucose is available in the quality required by the European Pharmacopoeia 1997 and is relatively inexpensive. Furthermore, the inventors have found that anhydrous glucose forms a cake when water is added to it which prevents effective dissolution. It is believed that a relatively large particle size is also advantageous in terms of effective dissolution, since large particle size results in improved flowability and less caking.

[0304] Figure 15 shows a sectional view through the lower part of the glucose compartment 420 of the disposable concentrate container 402 in position above the manifold 404, which illustrates the relative positions of the container 402, cap 406 and manifold 404 when the container 402 is loaded into the apparatus 100. The container 402 is loaded into the apparatus 100 by sliding it horizontally along a pair of container support rails 417. The container support rails 417 engage with projections 419 on the connectors 407 of the

container 402 so that the container support rails 417 hold the container 402 in a vertical position. The container support rails 417 are driven by the connection motor 422, see Fig. 5, in the vertical direction to raise or lower the container 402. It should be noted that when the disposable concentrate container 402 is loaded into the apparatus 100, the cap 406 closes off the manifold 404 to prevent outside contamination of the manifold 404 while the interior of the apparatus 100 is necessarily open to the atmosphere. Once the container 402 is loaded into the apparatus 100, the connection motor 422 acts to drive the container 402 downwardly via-by means of the container support rails 417 onto the cap 406 to keep the cap 406 firmly in position on the manifold 404 during disinfection.

[0305] As shown in Figure 15, the manifold 404 includes a drainage port 441 through which fluid may be drained to a reservoir vent disinfection valve 498, as described below.

[0306] As shown in Figure 15, the connector 407 includes an insert 421 which fits inside the neck of the compartment 420 and retains a septum 423 of silicone rubber or thermoplastic elastomer which seals off the compartment 420 during storage. The insert 421 includes (part of) the projections 419 for engagement with the container support rails 417 and is welded into the neck of the compartment 420. The connectors 407 of each of the compartments, 408- through 420, are all constructed in the same manner.

[0307] Within the compartment 420, a central pipe 425 runs up to the top of the compartment 420, although this is not shown in Figure 15. Each compartment, 408- through 420, has a central pipe 425 which functions as the air vent channel 424, the combined air vent and fluid channel 428, the glucose output channel 436 or the glucose air vent channel 432 depending on the particular compartment, 408- through 420.

[0308] At its upper end (not shown) the central pipe 425 may be received in an annular projection from the compartment lid 415 which is of a larger diameter than the central pipe

425 and circumscribes the central pipe 425. The gap between the annular projection and the wall of the central pipe 425 may act as a filter.

[0309] Alternatively, the central pipe 425 may be provided with an injection moulded filter element 439 as shown in Figure 23.

[0310] Between the base of the central pipe 425 and the sloping floor of the compartment 420, a diffuser 427 is provided in the form of a series of spaced bars extending radially outwardly from the central pipe 425 to the floor of the compartment 420. The diffuser 427 is shown in more detail in Figure 22. The diffuser 427 supports the central pipe 425 in the compartment 420 and also diffuses the flow of water (or other fluid) into the compartment 420 so that the flow is turbulent which agitates the powdered salt (or glucose) in the compartment 420 to aid dissolution. When the turbulent flow of water dissolves the powder in the region of the diffuser 427 the remaining powder falls down inside the compartment 420 so that all of the powder is dissolved.

[0311] In general, each of the compartments, 408- through 420, is constructed in this way. In one possible arrangement (not shown) the glucose compartment 420 has tapered sides extending outwardly in the upward direction which prevent the glucose powder in the compartment from lifting up when water is added. If there is a tendency for the powder to lift, a water channel is formed at the periphery of the compartment. The water dissolves any powder in this region, resulting in that the powder falls down and seals the channel.

[0312] As shown in Figure 15, the manifold 404 comprises a respective spike 429 for each connector 407. The spike 429 is arranged to break through the septum 423 to establish fluid communication between the manifold 404 and the compartment 420. The spike 429 is removably located in the manifold 404 and is intended to be replaced when it has been worn down by successive septa penetrations.

[0313] The spike 429 has a central fluid channel 431

defined therein which connects to the central pipe 425 of the compartment 420 (Figure 17). A further fluid channel 433 is also defined in the spike 429 and, when the container 402 is fitted to the manifold 404, is in fluid communication with the interior of the compartment 420 ~~via~~through the diffuser 427. Thus, the central fluid channel 431 and the central pipe 425 form a combined fluid channel which is concentric with the fluid channel formed by the neck of the connector 407. The type of spike 429 shown in Figure 15 is used to connect to the sodium bicarbonate compartment 412 and the sodium chloride compartment 414 and also the first connector 407a of the glucose compartment 420 to form the fluid input channel 434 and the glucose output channel 436.

[0314] An alternative spike 429a is shown in Figure 18. In this form of spike 429a, the central fluid channel 431a connects the central pipe 425 of the compartment 418 directly to atmosphere so that the central pipe 425 acts as an air vent. This type of spike is used to connect the lactic acid compartment 408, the cleaning agent compartment 410, the calcium chloride compartment 416 and the magnesium chloride compartment 418 to the manifold 404 and also to connect to the second connector 407b of the glucose compartment 420, to form the glucose air vent channel 432.

[0315] As shown in Figure 18, the cap 406 includes a cover portion 435 which fits over the spike 429a when the cap 406 is in position over the manifold 404 for disinfection of the apparatus 100. The cover portion 435 redirects a flow of disinfection fluid which emerges from the further fluid channel 433 back into the central fluid channel 431a, so that the central fluid channel 431a is disinfected. If the cover portion 435 were not present, it would not be possible to direct disinfection fluid through the further fluid channel 433 into the central fluid channel 431a.

[0316] Figure 16 shows the manifold cap 406 removed from the manifold 404. To achieve this from the position shown in Figure 15, the container 402 is lifted by means of the

container support rails 417 so that the cap 406 can pivot into the position shown in Figure 16. The cap 406 is attached to the manifold 404 by a spring-biased hinge 437 which ensures that the last part of the cap's movement onto the manifold 404 is linear, rather than rotational, so that there is no lateral abrasion of the seals between the manifold 404 and cap 406. A small D.C. motor (not shown) in the hinge 437 provides the motive power to rotate the cap 406 into and out of position on the manifold 404. Alternatively, a spring mechanism may be used.

[0317] Figure 17 shows the container 402 in position on the manifold 404, with the septum 423 broken by the spike 429.

[0318] Figure 24 and Figure 25 show an alternative design of the compartments, for example compartment 408 or 418. Below, compartment 408 will be described. The design differs from the design described in connection with Figures 13 - 18 mainly in the arrangement of the air vent channel 424 and the fluid channel 426.

[0319] The neck portion of the compartment 408 comprises an insert 542 having a membrane 545 attached to its upper surface. The membrane 545 is for example an aluminium foil, which may be broken and penetrated by a spike 429. The central channel of the spike co-operates with the air vent channel 424 as in the previous designs.

[0320] Integral with the air vent channel 424 is arranged a first tube 544. The first tube may have a circular cross section but any shape is possible. Inside the first tube 544 is arranged a second tube 546 leaving a small space 548 to the first tube 544. At the bottom of first tube 544, the small space 548 opens to the interior of the compartment 408 in a narrow ring-shaped slit 550. The second tube 546 is at the top thereof provided with a hole 552 communicating the interior of the second tube with saidthe small space 548. At the bottom thereof, the second tube 546 is connected to the ring-shaped channel of the spike 429 as shown.

[0321] In operation, in case of a compartment comprising

powder which should be primed, water is entered via-by means of spike 429 into second tube 546 up to the top thereof. Water passes out through hole 552 to the small space 548 and flows down to the ring-shaped slit 550 from where it is directed sideways along the bottom surface of the compartment to prime and, if applicable, dissolve the powder in the compartment. The small space still maintain most of its air content, since water is passed slowly down along the exterior surface of the second tube 546 and along the interior surface of first tube 544.

[0322] After priming and when fluid is to be taken out from the compartment, a suction is exerted by the spike inside tube 546. Fluid is sucked via slit 550 and upwards in the small space 548 to opening 552. The air in the small slit is moved down the upper portion of the second tube 546 but maintain entrapped there. Fluid fills the rest of the second tube 546. Since the flow is slow in the second tube 546, the air stays in the upper portion.

[0323] If the compartment is disengaged from the spike, the fluid in the second tube 546 is given off to the manifold portion 404 (figure 5). The air cushion in the upper portion of the second tube 546 prevents further fluid to pass upwards in the small space 548, and no further fluid may pass out from the compartment. Thus, drips from the cartridge is prevented, apart from the first few drips at disengagement. In this design, the septum 423 used in the previously described design is no longer necessary.

[0324] Figure 25 shows the same compartment as if figure 24 with the spike in the engaged position.

[0325] This design may be used with the lactic acid compartment 408, which is in liquid form from the start. The same design may also be used for the other compartments enclosing powder components, inclusive the glucose compartment.

[0326] Returning to Figure 5, in normal operation of the concentrate mixing module 400, heated purified water from the

thermal control and ~~sterilisation~~sterilization module 300 enters the concentrate mixing module 400 through the mixing water feed connection 4a. A mixing system bypass valve 440 allows the purified water to be output through the mixing module output connection 4b without being processed by the concentrate mixing module 400, for example for ~~sterilisation~~sterilization of downstream components. The water flow into the mixing system may be stopped by a mixing water stop valve 442.

[0327] Downstream of the mixing water stop valve 442 a glucose selector valve 444 is arranged to either allow the purified water to pass or to stop the flow of purified water and pass glucose solution from the glucose compartment 420 to the downstream components of the mixing system. In order to supply water to the glucose compartment 420 for dissolving the glucose, the mixing system bypass valve 440 is opened and a reversible flow control pump 446 is used to draw purified water from the mixing water feed connection 4a and pump it through the glucose selector valve 444 to the glucose compartment 420 via the glucose input valve 490 and fluid input channel 434. The flow control pump 446 is a piston pump of similar construction to the Gambro standard part No. K1 4207 002 but having a 9 mm or 12 mm diameter, rather than the standard 6 mm diameter. A glucose recirculation pump 448, for example a gear pump or a centrifugal pump, recirculates the water through the glucose compartment 420 ~~via~~by means of the fluid input channel 434 and the glucose output channel 436, to ensure total dissolution of the glucose. During recirculation, the glucose input valve 490 is closed and the rest of the mixing module 400 can therefore operate independently while the glucose is being dissolved.

[0328] Downstream of the glucose selector valve 444 a mixing chamber 450 mixes the flow of purified water from the mixing water feed connection 4a (or glucose solution from the glucose compartment 420) with the flow from a reversible salt input displacement pump 452 (Gambro standard part K1 4207

002).

[0329] The flow control pump 446 is provided with a tachometer 454, and the salt input displacement pump 452 is also provided with a tachometer 456. The tachometers, 454, through 456, monitor the volume flow rates of the respective pumps, 446, through 452, in order to verify correct operation. When a pumping operation is carried out solely under control of the salt input displacement pump 452, the flow control pump 446 is bypassed by opening a flow control pump bypass valve 458. Both the salt input displacement pump 452 and the flow control pump 446 are piston pumps which have the necessary volumetric accuracy to control the salt concentration of the PD fluid. The maximum flow rate through the salt input displacement pump 452 is for example 50 ml/min and the maximum flow rate through the flow control pump 446 is for example 180 ml/min.

[0330] Downstream of the flow control pump 446, two independent mixing conductivity meters 460 monitor the composition of the salt solutions passing there through, in combination with respective independent mixing temperature sensors 462. The two conductivity meters 460 and two temperature sensors 462 are provided for redundancy in the event of the failure of one meter or sensor. One of the meters and one of the temperature sensors communicates with the control system and the other meter and sensor communicate with the protective system, see Fig. 1a.

[0331] Downstream of the mixing conductivity meters 460 and the mixing temperature sensors 462, a drain disinfection valve 464 allows water from the mixing water feed connection 4a to be passed to the mixing module drain connection 15. The drain disinfection valve 464 is activated in this way during disinfection. In this case, the water entering the mixing water feed connection 4a has been heated to disinfection temperature by the thermal control and ~~sterilisation~~sterilization module 300 and is then passed to the drainage module 500 ~~via~~ by means of the drain disinfection

valve 464 to disinfect the drainage module 500.

[0332] A reservoir filling valve 466 directs the fluid passing through the mixing conductivity meters 460 either to the mixing module output connection 4b or to a concentrate reservoir 468, which is used to store the concentrated PD fluid before it is diluted by a controlled flow of purified water. The concentrate reservoir 468 has a reservoir output valve 470 through which the concentrated PD fluid may be passed to the salt input displacement pump 452.

[0333] The concentrate reservoir 468 also has a reservoir air vent connection 472 which can be opened to atmosphere at the manifold cap 406 under the control of a reservoir air vent valve 496 to vent air during filling or emptying of the concentrate reservoir 468. Because the concentrate reservoir 468 contains concentrated PD fluid which will be supplied to the patient, the reservoir air vent connection 472 is disinfected. In order to achieve this and to disinfect the spikes 429, during disinfection, the manifold cap 406 is lowered onto the manifold 404 to form a sealed cavity as shown in Figure 15. This cavity can be filled with hot disinfecting fluid from the thermal control and ~~sterilisation~~sterilization module 300 ~~via—by means of the~~ mixing water feed connection 4a, as described in detail below. The air which is initially contained within the cavity formed by the manifold 404 and the cap 406 is passed to the drainage module 500 through the mixing module drain connection 15 ~~via—by means of~~ a cap air vent valve 474. Once all the air has been vented from this cavity, the cap air vent valve 474 provides a connection from the cavity formed by the manifold 404 and the manifold cap 406 to the mixing module drain connection 15 so that disinfection fluid can be circulated through the cavity. In this way, the reservoir air vent connection 472 can be completely disinfected, even though in operation of the system the reservoir air vent connection 472 is open to atmosphere. The reservoir air vent valve 496 is closed during this process, but can be opened once the manifold 404 and manifold cap 406

have been disinfected to pass disinfection fluid from the reservoir air vent connection 472 directly to the mixing module drain connection 15 to disinfect the reservoir air vent valve 496. The cavity formed by the manifold 404 and the manifold cap 406 is drained after disinfection by connecting the cavity to atmosphere at the manifold cap air vent 6 by opening the cap air vent valve 474. Disinfection fluid is then able to drain to the drainage module 500 via the reservoir vent disinfection valve 498, the reservoir air vent valve 496 and the mixing module drain connection 15.

[0334] The dissolution and mixing of the salts from the compartments of the disposable concentrate container 402 is effected by the opening and closing of the valves on the fluid lines, 426_T and 430_L of the compartments, 408- through 418, such that the salt input displacement pump 452 in a priming step can supply water to, and subsequently withdraw salt solution from, each of the compartments, 408- through 418.

[0335] Each compartment, 408- through 418, of the disposable concentrate container 402 is provided with a respective input valve, namely a lactic acid input valve 478, a cleaning agent input valve 480, a sodium bicarbonate input valve 482, a sodium chloride input valve 484, a calcium chloride input valve 486 and a magnesium chloride input valve 488. In addition, the function of the combined air vent and fluid channels 428 of the sodium bicarbonate compartment 412 and the sodium chloride compartment 414 is controlled by a sodium bicarbonate air vent valve 492 and a sodium chloride air vent valve 494, respectively.

[0336] The correct operation of these valves, 478- through 488, is monitored using a salt input pressure sensor 476 in the following manner. After one of the input valves, 478- through 488, has been operated and is closed, a signal is sent to all of the input valves, 478- through 488, to close the valves. The salt input displacement pump 452 is then energised to pump water from the mixing water feed connection 4a towards the input valves, 478- through 488. The pressure generated by

the salt input displacement pump 452 is monitored by the salt input pressure sensor 476. In the event that one of the input valves, 478- through 488, is stuck in the open position, a sufficiently high pressure will not be attainable and this fault condition will be detected by the salt input pressure sensor 476.

[0337] In the case of the first type of compartment, 408, 410, 416, and 418, described above and taking the calcium chloride compartment 416 as an example, water from the mixing water feed connection 4a is drawn by the salt input displacement pump 452 through the mixing chamber 450 and is pumped through the calcium chloride input valve 486 into the calcium chloride compartment 416 via the fluid channel 426 of that compartment. All other input valves, 478- through 488, of the other compartments, 408- through 418, are closed. The air in the calcium chloride compartment 416 which is displaced by the water pumped into that compartment is vented to atmosphere through the air vent channel 424.

[0338] When the salt input displacement pump 452 has passed the required amount of water into the calcium chloride compartment 416, it is expected that all the calcium chloride powder that was in the compartment when the disposable concentrate container was loaded has been dissolved. The weight of calcium chloride in the calcium chloride compartment 416 is predetermined and the volume of water passed by the salt input displacement pump 452 is known, such that an approximation of the concentration of the calcium chloride solution formed in the calcium chloride compartment 416 can be derived.

[0339] The displacement pump 452 is driven by a step motor. Each step corresponds to a well defined volume of fluid pumped, dependent on the rotational position of the step motor. The control system of the pump motor calculates the volume pumped by the pump in an accurate manner.

[0340] In order to transfer the necessary amount of calcium chloride solution to the concentrate reservoir 468, the flow

control pump 446 is activated to draw water from the mixing water feed connection 4a at a predefined rate. The water is directed to the mixing module drain connection 15 by the drain disinfection valve 464. The salt input displacement pump 452 is activated to pump the calcium chloride solution at a controlled volume flow rate through the mixing chamber 450 via the flow control pump 446 through the mixing conductivity meters 460 to the mixing module drain connection 15. The flow rate through the mixing water feed connection 4a is reduced by an amount equal to the flow rate generated by the salt input displacement pump 452 because the flow rate through the flow control pump 446 is constant, whereby a predetermined dilution ratio is obtained. The mixing conductivity meters 460 measures the conductivity, and thus the concentration, of the diluted calcium chloride solution and the flow rate of the salt input displacement pump 452 is adjusted to achieve a predetermined concentration. Once the concentration is achieved, the drain disinfection valve 464 is switched and the reservoir filling valve 466 directs the calcium chloride solution to the concentrate reservoir 468, where it is stored until all the components of the concentrated PD fluid have been prepared. The total volume and the concentration of the calcium chloride solution which has passed through the flow control pump 446 into the concentrate reservoir 468 is therefore known and thus the amount of calcium chloride present in the concentrate reservoir. It is noted that the order of introduction of salts is closer described below.

[0341] A similar process to that for the dissolution and measurement of the calcium chloride solution is used for the preparation of the magnesium chloride solution from the magnesium chloride compartment 418. The cleaning agent is also dissolved in the cleaning agent compartment 410 in this way, when required. The lactic acid is routed to the concentrate reservoir 468 without dilution. As explained below, the solution created with the cleaning agent is not a component of the PD fluid.

[0342] The solutions of sodium bicarbonate and sodium chloride are produced in a different manner to those for magnesium chloride and calcium chloride, because sodium bicarbonate and sodium chloride are used in greater amounts than magnesium chloride and calcium chloride. Taking as an example the preparation of sodium bicarbonate, all of the input valves, 478- through 488, are closed, except for the sodium bicarbonate input valve 482. The sodium bicarbonate air vent valve 492 is set such that the combined air vent and fluid channel 428 of the sodium bicarbonate compartment 412 is connected to atmosphere via-by means of the manifold 404. The salt input displacement pump 452 pumps a measured quantity of water from the mixing water feed connection 4a via-by means of the mixing chamber 450 through the sodium bicarbonate input valve 482 and into the sodium bicarbonate compartment 412 via by means of the combined priming and output channel 430. Sufficient water is introduced into the sodium bicarbonate compartment 412 that the sodium bicarbonate powder in the compartment 412 is fully immersed in water.

[0343] Once the sodium bicarbonate powder in the sodium bicarbonate compartment 412 is fully immersed the sodium bicarbonate air vent valve 492 is switched to provide a fluid path from the mixing water feed connection 4a to the combined air vent and fluid channel 428 of the sodium bicarbonate compartment 412. The salt input displacement pump 452 is reversed and draws a substantially saturated sodium bicarbonate solution out of the sodium bicarbonate compartment 412 through the combined priming and output channel 430 and the sodium bicarbonate input valve 482. The conductivity of the sodium bicarbonate solution is controlled and the solution is diluted and stored in the concentrate reservoir 468 in the same manner as for the calcium chloride solution described above.

[0344] The mixing and measuring of the sodium chloride solution is carried out in a corresponding manner.

[0345] The amounts of salt in each of the compartments,

408- through 418, are chosen such that in correct operation each compartment, 408- through 418, produces a salt solution with a characteristic conductivity. Thus, if a malfunction of the system occurs whereby the wrong salt solution, for example magnesium chloride instead of calcium chloride, is produced, this will be identifiable from the conductivity measurement.

[0346] Furthermore, the salts are mixed at relatively high concentrations which provides an environment in which bacteria are unable to survive and thereby aids bacteriological control. The relatively high concentrations also allow the conductivity meters 460 to operate in a range in which measurement errors are relatively insignificant compared to the measured values, thereby increasing the accuracy of the concentration measurements.

[0347] The dissolution of the glucose solution has been described above. A required amount of the glucose solution is pumped to the concentrate reservoir 468 via-by means of the glucose input valve 490, glucose selector valve 444 and the reservoir filling valve 466 by the flow control pump 446. This pump is used because it has a high capacity, whereby the metering of the glucose may take place in a shorter time.

[0348] At the end of the dissolution and measuring operation, the concentrate reservoir 468 contains concentrated PD fluid with the correct relative proportions of salts and glucose required by the patient's individual prescription but at a higher absolute concentration. Thus, it is then only necessary to add water to this concentrated PD fluid to obtain PD fluid according to the patient's prescription.

[0349] When it is desired to provide the PD fluid to the patient through the mixing module output connection 4b, a measured flow (around 50 ml/min) of concentrated PD fluid is drawn from the concentrate reservoir 468 via-by means of the reservoir output valve 470 by the salt input displacement pump 452, which pumps the concentrated PD fluid into the mixing chamber 450. The flow control pump 446 is bypassed by opening a flow control pump bypass valve 458 and a constant flow

(around 300 ml/min) of PD fluid is drawn out of the mixing module output connection 4b by the volumetric pump 352 of the thermal control and ~~sterilisation~~sterilization module 300, see figure 4. The flow out of the mixing module output connection 4b is greater than that produced by the salt input displacement pump 452, and the additional fluid flow (around 250 ml/min) that is not provided by the salt input displacement pump 452 is drawn from the mixing water feed connection 4a. In this way, the concentrated PD fluid from the concentrate reservoir 468 is diluted in the mixing chamber 450 with water from the mixing water feed connection 4a so that PD fluid at the desired concentration exits the concentrate mixing module 400 via the mixing module output connection 4b. The concentration of the PD fluid is monitored by the mixing conductivity meters 460 and is controlled by varying the flow rate through the salt input displacement pump 452.

[0350] The dilution of the concentrated PD fluid from the concentrate reservoir 468 in this way not only reduces the salt and glucose concentration of the PD fluid to the required level, but also ensures that the level of dissolved gas in the PD fluid is low and below the medically required maximum level. The inventors have assumed that by the time the concentrated PD fluid in the concentrate reservoir 468 is ready for use it will be, at most, saturated with dissolved gas which has entered the system during dissolution of the salts and glucose. However, the water entering the concentrate mixing module 400 at the mixing water feed connection 4a has been degassed by the water preparation module 200. The dilution ratio of the flows of the concentrated dialysis fluid pumped by the salt input displacement pump 452 and the water entering the mixing water feed connection 4a has been chosen to be at least sufficient to dilute the gas-saturated concentrated dialysis fluid to a dissolved gas content below the medically required level.

[0351] The flow through the RO membrane disinfection connection 3 is controlled by an RO membrane disinfection

valve 499. During disinfection, water at disinfection temperature is supplied to the mixing water feed connection 4a by the thermal control and ~~sterilisation~~sterilization module 300 and is pumped by the salt input displacement pump 452 through the mixing water stop valve 442, the glucose selector valve 444, the mixing chamber 450 and the RO membrane disinfection valve 499 via the RO membrane disinfection connection 3 to the water preparation module 200.

[0352] After the concentrate disposable container 402 is put in place and into engagement with the spikes 429 in the manifold 404, the following sequence of operations takes place.

[0353] First, the cleaning agent compartment 410 is primed with water by the introduction of 80 ml of water into the cleaning agent compartment 410, which comprises 20 g sodium carbonate, in order to thereby produce a sodium carbonate solution having a concentration of about 2284 mmol/l. The sodium carbonate solution is used for cleaning purpose as described above.

[0354] The peritoneal dialysis fluid is composed of six separate substances namely magnesium chloride, calcium chloride, sodium bicarbonate, sodium chloride, lactic acid and glucose. The amount of material in each compartment, 410 through 420, is given in Table 2.

[0355] In order to prime the disposable concentrate container 402, firstly 962 ml of water is introduced into the glucose compartment 420 by the flow control pump 446. Since the flow control pump 446 can operate at about 180 ml/min, this introduction will take approximately 5.5 minutes. Then the glucose input valve 490 is closed and the glucose recirculation pump 448 is operated in order to recirculate the glucose in the glucose compartment 420 to promote full dissolution.

[0356] Thereafter, the magnesium chloride input valve 488 is opened to introduce 48.4 ml of water into the magnesium chloride compartment 418. Then the magnesium chloride input

valve 488 is closed and the calcium chloride input valve 486 is opened to introduce 145.2 ml of water into the calcium chloride compartment 416. These introductions of water are performed by the salt input displacement pump 452, which has a maximum capacity of about 50 ml/min. The above two priming steps will take about 4 minutes together. The magnesium chloride and the calcium chloride are fully dissolved in the water introduced, either during the introduction of water into the compartment or shortly thereafter to finally dissolve all of the salt particles.

[0357] Then the water is introduced into the sodium bicarbonate compartment 412 by opening the sodium bicarbonate input valve 482 and introducing about 60 ml of water by means of the salt input displacement pump 452. The exact amount of water introduced into the sodium bicarbonate compartment 412 is not crucial provided the water level does not rise above the combined air vent and fluid channel 428 so that water is not passed down that channel 428 to the manifold 404 via-by means of the sodium bicarbonate air vent valve 492. If a small portion of the water nevertheless does pass this way, this is of no consequence.

[0358] The same procedure is performed for the sodium chloride compartment 414 by the introduction of approximately 100 ml of water into the compartment by means of the salt input displacement pump 452. All of the powder in the sodium bicarbonate compartment 412 and the sodium chloride compartment 414 is not completely dissolved, because the water quantity is insufficient to dissolve all of the powder.

[0359] No water is added to the lactic acid compartment 408, which comprises 120 g lactic acid having a concentration of 30%.

[0360] By means of the above described priming procedure, the different compartments, 408- through 420, will comprise electrolyte solutions of the salts and glucose having the following concentrations when taken out from the respective compartments at 25°C:

magnesium chloride	2455.8 mmol/l
calcium chloride	2117.3 mmol/l
sodium bicarbonate	1199 mmol/l
sodium chloride	5253 mmol/l
lactic acid	3500 mmol/l
Glucose	3393.6 mmol/l

[0361] The exact order of priming of the compartments may differ from the order given above.

[0362] The next step in the procedure is to transfer measured amounts of the electrolytes and the glucose to the concentrate reservoir 468. The resulting solution in the concentrate reservoir 468 may be a solution having five times the concentration of the final required solution. The concentrate reservoir solution is then diluted by 1:5 before being sent to the OLA 375 for ~~sterilisation~~sterilization before introduction into the peritoneal cavity of the patient. Thus, the concentrate reservoir 468 should comprise 600 ml of concentrated solution in order to provide 3000 ml of final peritoneal dialysis solution after dilution.

[0363] The first substance to be introduced into the concentrate reservoir 468 is sodium bicarbonate. The sodium bicarbonate air vent valve 492 is adjusted to connect the combined air vent and fluid channel 428 with the mixing water feed connection 4a and the sodium bicarbonate input valve 482 is opened to connect the combined priming and output channel 430 with the salt input displacement pump 452. By operating the salt input displacement pump 452, substantially saturated sodium bicarbonate solution is taken out from the bottom of the sodium bicarbonate compartment 412 and water from the water preparation module 200 is introduced into the top of the sodium bicarbonate compartment 412 via the combined air vent and fluid channel 428. In order to provide a bicarbonate concentration of 40 mmol/l in the final solution, it is required to transfer 120 mmol of sodium bicarbonate to the concentrate reservoir 468, which corresponds to 100 ml pumped by the salt input displacement pump 452. Thus, the salt input

displacement pump 452 may be operated at a pump speed of 40 ml/min in 2.5 minutes in order to provide the required amount. At the same time the flow control pump 446 is adjusted to 60 ml/min in order obtain a dilution ratio of 1:1.5 resulting in a conductivity of approximately 35 mS/cm.

[0364] As described before, the mixed solution is passed to the drainage module 500 via-by means of the drain disinfection valve 464 and the mixing module drain connection 15 until a stable value has been obtained from the mixing conductivity meters 460. Then the drain disinfection valve 464 and the reservoir filling valve 466 are switched over in order to transfer the solution to the concentrate reservoir 466.

[0365] The conductivity measurement at the mixing conductivity meters 460 is converted to the corresponding concentration of sodium bicarbonate by the control system and is multiplied by the flow velocity as measured by tachometer 454 of the flow control pump 446 to thereby obtain the amount of sodium bicarbonate per minute passing through the mixing conductivity meters 460. By integrating this amount per minute over time, the total amount of material delivered to the concentrate reservoir 468 is obtained. When 120 mmol have been transferred, the reservoir filling valve 464 is switched over in order to stop further introduction into the concentrate reservoir 468 and direct the solution to the drainage module 500 via-by means of the mixing module drain connection 15. The fact that the correct amount of material has been delivered to the concentrate reservoir 468 can also be controlled by the tachometer 456 of the salt input displacement pump 452, which should pump 100 ml.

[0366] Immediately after the shifting over of the reservoir filling valve 464, the salt input displacement pump 452 is reversed to pump clean water in the opposite direction to push back the sodium bicarbonate present in the tubes between the sodium bicarbonate input valve 482 and the mixing chamber 450, in order to save material and also in order to flush the tube system with clean water. The volume of substantially saturated

sodium bicarbonate so recovered is relative small, but may still be significant. A corresponding volume of air is transferred into combined air vent and fluid channel 428 since there is normally an air cushion at the top of compartment 412. During the next operation of the compartment, this air volume is reintroduced into compartment 412.

[0367] The flow control pump 446 operates to flush the rest of the pipe system downstream of the mixing chamber 450 of any sodium bicarbonate.

[0368] If the peritoneal dialysis fluid is to comprise substantially only bicarbonate as buffer, the final concentration of the buffer can be adjusted by the adjustment of the amount of bicarbonate introduced into the concentrate reservoir 468. Introduction of 100 ml will result in a final bicarbonate concentration of 40 mmol/l and introduction of 87.5 ml will result in a final bicarbonate concentration of 35 mmol/l. The pH may be adjusted by the addition of lactic acid.

[0369] If the final peritoneal dialysis fluid is to comprise a mixture of sodium bicarbonate and sodium lactate, for example 25 mmol/l bicarbonate and 15 mmol/l sodium lactate, the following procedure is followed. Any mixture from about 5:35 to 35:5 can be obtained or any other total sum than 40.

[0370] The lactic acid input valve 478 is opened to connect the lactic acid compartment 408 with the salt input displacement pump 452. The mixing water stop valve 442 is closed to prevent dilution of the lactic acid and the flow control pump bypass valve 458 is opened to bypass the flow control pump 446. If 15 mmol/l of sodium lactate is desired, the salt input displacement pump 452 pumps 16 ml of lactic acid (30% concentration) into the concentrate reservoir 468. The concentration of the lactic acid solution may be monitored by the mixing conductivity meters 460, which should show a conductivity value of approximately 39 mS/cm.

[0371] During the introduction of lactic acid into the bicarbonate solution in the concentrate reservoir 468, the

acid reacts with the bicarbonate ions and forms carbon dioxide, which is vented to atmosphere via the reservoir air vent connection 472, the reservoir air vent valve 496 and the cap air vent valve 474. At the top of the concentrate reservoir 468, a cushion of carbon dioxide is formed, which is not transferred to the surrounding atmosphere. Thus, the carbon dioxide partial pressure will be one atmosphere (1 Bar) which results in a dissolved carbon dioxide concentration of about 23 mmol/l at equilibrium in the liquid in the concentrate reservoir. The formation of carbon dioxide is comparatively fast, but a short pause may be required until the carbon dioxide generation has ceased.

[0372] Once again the salt input displacement pump 452 is reversed for pushing back the lactic acid into the lactic acid compartment 408 until water reaches the lactic acid input valve 478 or shortly there before, and the tube system is flushed with water ~~via~~ by means of the flow control pump 446.

[0373] Next, sodium chloride is introduced into the concentrate reservoir 468. In order to provide 140 mmol/l in the final solution, 470 mmol has to be transferred to the concentrate reservoir 468, which corresponds to 80 ml of concentrated solution. Since sodium chloride has a very high conductivity, the sodium chloride is diluted as much as possible in the mixing chamber 450. However, the dilution can not be too large because of restrictions in the final volume in the concentrate reservoir 468. As an example a dilution ratio of 1:4 is given below. Thus, the flow control pump 446 is adjusted to 40 ml/minute and the salt input displacement pump 452 is adjusted to 160 ml/min resulting in a conductivity of about 98 mS/cm. The same integration method as described above for sodium bicarbonate is used in order to determine when a sufficient amount of sodium chloride has been introduced into the concentrate reservoir 468. Alternatively, it is determined when the salt input displacement pump 452 has pumped 80 ml, which should be approximately after two minutes.

[0374] Again the salt input displacement pump 452 is

reversed to push back the sodium chloride solution into the sodium chloride compartment 414 and some air into combined air vent and fluid channel 428.

[0375] Then, the glucose input valve 490 is opened to transfer glucose to the concentrate reservoir 468. If 1.5% final glucose concentration is to be obtained, 75 ml glucose solution should be transferred, if 2.5% is to be obtained, 125 ml should be transferred, and if 4.0% is to be obtained, 200 ml should be transferred. In order to save time, the flow control pump 446 is used for this purpose. Glucose has no inherent conductivity, which is checked by the mixing conductivity meters 460. When the correct amount has been introduced as measured by tachometer 454, the glucose selector valve 444 is operated to transfer water from the mixing water feed connection 4a via the flow control pump 446 to flush the tube system. The flow control pump 446 may first be reversed while the mixing system bypass valve 440 is opened to push back glucose to the glucose compartment 420 as described above, if desired. Since the recovered volume is small compared to the volume in the glucose department, the recovery may not be used for glucose.

[0376] The dilution ratio of sodium chloride is selected in dependence on the desired glucose concentration so that the volume obtained in the concentrate reservoir 468 so far is approximately 570 ml.

[0377] Finally, magnesium and calcium are introduced into the concentrate reservoir 468. These substances are introduced as late as possible when the bicarbonate is diluted to a low concentration to avoid problems with precipitation.

[0378] First magnesium chloride is introduced by opening the magnesium chloride input valve 488 and operating the salt input displacement pump 452. Only 1.5 mmol magnesium chloride should be transferred by the salt input displacement pump 452, which corresponds to 0.6 ml, to obtain a final concentration of 0.5 mmol/l. The salt input displacement pump 452 is able to meter such small quantities with sufficient accuracy. The pump

has a displacement of 228 ~~microlitre~~-microliter per revolution and is controlled over 1/100 revolution.

[0379] Magnesium chloride is not introduced in concentrated form into the concentrate reservoir 468 to avoid local precipitation. Thus, the flow control pump 446 is operated with 10 times the speed of the salt input displacement pump 452 to obtain a dilution ratio of 1:10. Then the conductivity of the magnesium chloride solution will be around 35 mS/cm. By integrating the concentration obtained from the mixing conductivity meters 460 multiplied with the flow velocity obtained from the flow control pump 446, the delivered amount is obtained. The delivered amount is checked by the salt input displacement pump 452, which should pump 0.6 ml. After completion of the introduction into the concentrate reservoir 468, the salt input displacement pump 452 is reversed to push back magnesium chloride into the magnesium chloride compartment 418. This procedure is of importance for magnesium chloride and calcium chloride, which are provided in small quantities.

[0380] Finally, the same procedure is performed for calcium chloride. In order to provide 1.5 mmol/l calcium in the final solution, it is necessary to transfer 4.5 mmol corresponding to 2.1 ml concentrated solution to the concentrate reservoir 468. As for magnesium, this process is performed by dilution in the ratio of 1:10. The conductivity will then be approximately 34 mS/cm.

[0381] When calcium ions are mixed with bicarbonate ions, there is always a risk of calcium carbonate precipitation. By keeping an air cushion comprising carbon dioxide above the surface of the concentrate reservoir 468 and thereby providing a saturated carbon dioxide gas content in the solution, it is assured that the pH of the solution is as low as possible, whereby no precipitation will take place.

[0382] To assure the highest possible content of carbon dioxide before mixture with calcium chloride, lactic acid may be introduced as late as possible in the mixing procedure,

i.e. immediately before the addition of magnesium chloride and calcium chloride, to obtain carbon dioxide generation and saturation of the complete solution with carbon dioxide. The order of sodium bicarbonate, sodium chloride and glucose may also be different from that given above, for example first sodium chloride, then glucose and then sodium bicarbonate.

[0383] After the formation of the concentrated PD solution in the concentrate reservoir 468, it is diluted in the ratio of 1:5. In this mode of operation, the OLA pump 352 is operated at 300 ml/min and the salt input displacement pump 452 is operated at 60 ml/min to obtain a dilution ratio of 1:5. The mixing conductivity meters 460 control the concentration of the mixed solution and adjust the salt input displacement pump 452 to avoid variation in the conductivity.

[0384] A slightly modified mixing portion is disclosed in Figure 5a. A metering pump 448a is inserted in the pipe between the glucose input valve 490 and the glucose selector valve 444. The metering pump 446a is shunted by a valve 490a. The glucose selector valve 444 is replaced by a direct connection to the mixing chamber 450. These additional components enable the measurement of the glucose concentration in the glucose compartment 420. The operation is as follows.

[0385] After dissolution of the glucose in the water introduced into the glucose compartment 420, the glucose should have a concentration of 50%. However, there is always a risk of errors and there is a desire to be able to control the glucose concentration.

[0386] To start this glucose check procedure, the sodium chloride input valve 484 and the sodium chloride air vent valve 494 are opened, the salt input displacement pump 452 is operated and the flow control pump 446 is operated in order to provide a sodium chloride solution having a concentration of about 500 mmol/l, i.e. a dissolution ratio of about 1:10. The mixing conductivity meters 460 should measure approximately 46.7 mS/cm. The flow control pump 446 is operated at approximately 50 ml/min and the salt input displacement pump

452 at approximately 5 ml/min. Then the glucose input valve 490 is opened and the metering pump 448a is operated to pump glucose solution from the glucose compartment 420 via the fluid input channel 434, the glucose input valve 490 and the metering pump 448a into the mixing chamber 450. The metering pump 448a is driven at for example 20 ml/min.

[0387] The introduction of glucose into the sodium chloride solution in the mixing chamber 450 results in a decrease of the conductivity as measured by the mixing conductivity meters 460. The decrease is substantially proportional to the concentration of the glucose solution. Thus, the glucose concentration in the glucose compartment 420 can be monitored.

[0388] After measuring the glucose concentration, the above described procedure may take place.

[0389] Alternatively, the mixture obtained as described in relation to Figure 5a, i.e. a mixture of glucose and sodium chloride, may be transferred to the concentrate reservoir 468. In that case, the sodium salt input displacement 452 should have a higher speed to ensure that the amount of water introduced into the concentrate reservoir 468 is not too high.

[0390] It is possible to obtain the same operation by using the glucose recirculation pump 448 as a reversible metering pump instead of a separate metering pump 448a.

[0391] It would also be possible to use the lactic acid and dilute it with glucose to monitor the lowering of conductivity. In that case, no additional pump is required compared to Fig. 5. The operation would be to open the lactic acid input valve 478, adjust the salt input displacement pump 452 to 10 ml/min, adjust the flow control pump 446 to 15 ml/min, with the glucose selector valve 444 and the mixing water stop valve 442 open to permit 5 ml/min of water to pass into the mixing chamber 450 from the mixing water feed connection 4a. The conductivity is measured. Then, the glucose input valve 490 is opened and the glucose selector valve 444 is switched over to replace the water supply (5 ml/min) to the mixing chamber 450 with glucose. The decrease in conductivity

is monitored and a calculation is made to determine the corresponding concentration of glucose.

[0392] In Figure 5a there is shown an electric heater 438a in the fluid input channel 434 to glucose compartment 420 to heat the recirculated glucose solution during the dissolution process to promote dissolution. Glucose becomes cooler during dissolution and therefor needs heating to maintain a temperature of for example 40°C during the complete dissolution step.

[0393] Another alternative design of the glucose metering step is shown on Fig. 5b and Fig 4a. Turning first to Fig. 5b, the metering pump 448a has been replaced by a reversible metering pump 448b. Metering pump 448b is constructed to be able to pump the glucose solution against a back pressure of several bar, more than 3 bar and preferably more than 6 bar or reasons appearing below. A valve 490a bypasses the pump 448b. A glucose input valve 490b is arranged between mixing chamber 450 and inlet tube 434 to prime the glucose in compartment 420.

[0394] The operation of the alternative arrangement according to Fig. 5b is the same as described above in connection with Fig. 5 or Fig. 5a, except that the glucose is not entered in concentrate reservoir 468. Instead, the concentrated glucose is metered by metering pump 448b and transferred via the activated valve 490b to an outlet connection 4c, leading to an input connection in the middle of the OLA ~~sterilisersterilizer~~, as indicated on Fig. 4a.

[0395] In the alternative OLA ~~sterilisersterilizer~~ arrangement shown of Fig. 4a, the oil bath arrangement 364 - 368 is replaced by an electric heater 364a. The inlet fluid entering the OLA arrangement via inlet 4b, valve 356 and heat exchangers 360 and 362 is an electrolyte fluid having components which are not sensitive to heat. Thus, the electrolyte fluid may be heated with an electric heater without risk of decomposition or the formation of harmful substances, although an electric heater may have spots of high

temperature. The heat sensitive portion of the final solution, namely the glucose is entered after the electric heater 364a at inlet 4c. At this position, the electrolyte fluid is at a high temperature of for example 150°C and at a high pressure of for example 6 bar absolute pressure. The inlet fluid heats the concentrated glucose solution rapidly to a high temperature of for example 148°C. The combined fluid is maintained at a high temperature for a predetermined time period determined by the flow distance in a coil 363. Then, the combined fluid is cooled rapidly in heat exchangers 362 and 360. The temperature is monitored by temperature sensors 370. By this operation, the sensitive glucose portion is heated in a substantially square temperature curve, which is beneficial for the ~~sterilisation~~sterilization and for avoiding the formation of glucose degradation products. The ~~sterilisation~~sterilization of the glucose portion may be very well controlled in order not to over-~~sterilise~~sterilize the glucose. The fact that the electrolyte fluid may become slightly over-~~sterilise~~sterilized means no disadvantage.

[0396] It is possible to include calcium and magnesium ions in the glucose fluid to be late introduced in the OLA arrangement of Fig. 4a in order to avoid possible problems with calcium carbonate precipitation and scaling of the tube portions in the mixing arrangement of Fig. 5b. In this embodiment, calcium chloride and magnesium chloride is transferred to the glucose compartment 420 after the dissolution of the glucose but before the metering of the glucose to output connection 4b. Valve 486 is opened and pump 452 is operated to withdraw calcium chloride from compartment 424. Valve 442 and valve 458 are closed and pump 446 is inoperative. Valve 490 b is placed in the position shown on Fig. 5b and valve 490a is opened. The calcium chloride fluid metered by pump 452 must pass via mixing chamber 450 and valves 490b and 490a to the glucose compartment 420. The amount of calcium chloride transferred to glucose compartment 420 is carefully monitored by the metering pump 452. The same

operation takes place for magnesium chloride.

[0397] Finally, the combined glucose, calcium chloride and magnesium chloride is metered to output 4c to be included in the final PD fluid. By this arrangement, sodium bicarbonate and calcium chloride are not mixed until in the diluted PD fluid, which means that the risk of precipitation is minimised.

[0398] Alternatively, the calcium chloride may be metered by metering pump 452 to mixing chamber 450. Flow control pump 446 is operated to dilute the calcium chloride and the fluid is measured in conductivity meters 460. The measured and diluted calcium chloride is then transferred to glucose chamber via a valve 464a shown in broken lines in Fig. 5b. The same operation takes place with magnesium chloride.

[0399] Alternatively, or in combination, (part of) calcium chloride and/or magnesium chloride may be transferred to concentrate reservoir 468 as previously described.

[0400] Drainage Module 500

[0401] The drainage module 500 is shown in detail in Figure 6. The fluid supplied to the drainage module 500 by the ambient pressure drain connection 14b and the mixing module drain connection 15 is routed directly to the heat recovery drain connection 13b from which it passes to the thermal control and ~~sterilisation~~sterilization module 300 for heat recovery before being returned to the heat recovery drain return connection 13c. The fluid entering the heat recovery drain return connection 13c passes to the external waste connection 16 via-by means of a heat recovery return valve 532. The temperature of the fluid exiting the heat recovery drain connection 13b is monitored by a drain disinfection temperature sensor 530.

[0402] Water from the thermal drain connection 13a, which originates from the purification waste connection 2d of the water preparation module 200, passes through a thermal drain connection valve 520 directly to the external drain connection 16.

[0403] Fluid from the negative pressure drain connection 14a passes through a pressure conditioning chamber 510 under a negative pressure generated by a drainage pump 508 and then passes to the heat recovery drain connection 13b via-by means of the drain disinfection temperature sensor 530. The pressure conditioning chamber 510 is in the form of a chamber closed by a movable, spring-biased diaphragm, and is provided to prevent pressure fluctuations due to the drainage pump 508 from being passed to the patient along the negative pressure drain connection 14a, and also to make control of the draining process easier. The drainage pump may be a peristaltic pump or gear pump, or a pump generating a predetermined maximum pressure, like a centrifugal pump.

[0404] The conditioning chamber 510 moreover ensures that the patient is not exposed to large negative pressures. For this purpose, the conditioning chamber 510 may be provided with limit switches 512 and 514 that monitors the position of a spring loaded piston 516 in the chamber 510. The switches may be used for controlling the drainage pump 508 to provide a negative pressure compatible with safe patient conditions during drainage of the patient, such as not exceeding 1 meter of water pillar negative pressure in relation to the atmosphere.

[0405] For disinfection, hot disinfecting fluid enters the drainage module 500 through the mixing module drain connection 15, the negative pressure drain connection 14a and the ambient pressure drain connection 14b. The disinfecting fluid is passed from the drainage module 500 along the heat recovery drain connection 13b to the thermal control and ~~sterilisation~~sterilization module 300 via-by means of the drain disinfection temperature sensor 530. The heat from the disinfection fluid is recovered in the thermal control and ~~sterilisation~~sterilization module 300 and the fluid is returned to the drainage module 500 via-by means of the heat recovery drain return connection 13c which passes the fluid to the external waste connection 16 via-by means of the heat

recovery return valve 532. Chemical disinfectant (or hot water in the case of heat disinfection) from the water preparation module 200 enters the drainage module 500 through the thermal drain connection 13a and passes directly to the external drain connection 16.

[0406] Cycler and sterilisablesterilizable connector module 600

[0407] The cycler and sterilisablesterilizable connector module 600 is shown in detail in Figure 7. In normal operation, sterile PD fluid is provided to the cycler and sterilisablesterilizable connector module 600 via-by means of the sterile fluid connection 8a and passes through a patient fill valve 602 to a dialysate line sterilisablesterilizable connector 604. The sterilisablesterilizable connector 604 may be of the type described in International patent application WO96/05883 (Gambro AB) which is incorporated herein by reference.

[0408] The operation of the sterilisablesterilizable connector 604 is shown schematically in Figures 19a to 19d. Referring to Figure 19a, the sterilisablesterilizable connector 604 is arranged to receive a double male connector 630 at the end of the disposable fluid line 10 in two corresponding chambers 632. The end of each prong of the male connector 630 is closed by a pierceable membrane 634. The membranes 634 are pierced by respective membrane spikes 636 when the male connector 630 is fully inserted in the chambers 632, as shown in Figure 19c. The membrane spikes 636 have channels defined there through for fluid flow in the direction of the arrows in Figures 19b and 19c. The chambers 632 are connected by a fluid passage 638 which can be opened or closed by a connector valve 640. In an alternative embodiment, there is no connector valve 640, as shown in Fig. 19b.

[0409] Initially, the male connector 630 is partially inserted into the chambers 632 as shown in Figure 19b. The connector valve 640 is opened and water at sterilisationsterilization temperature and pressure (3 bar) is

circulated through the membrane spikes 636, the chambers 632 and the fluid passage 638 in the direction of the arrows in Figure 19b. The circulation of the ~~sterilising~~sterilizing water ~~sterilise~~sterilizes the chambers 632, the membranes 634 and the membrane spikes 636. Once this ~~sterilisation~~sterilization operation has been completed, the male connector 630 is inserted all the way into the chambers 632, so that the membranes 634 are pierced and a fluid path is opened through the membrane spikes and into the disposable dialysate line 10. At the same time, the fluid connection between the chamber 632 and the fluid passage 638, as well as an area around the spikes, is closed off by the male connector 630. Fluid, for example PD fluid, can then flow in the direction of the arrows shown in Figure 19c during a rinsing step or for filling and draining a peritoneal cavity of a patient.

[0410] At the end of the treatment session, the flow of PD fluid into the ~~sterilisable~~sterilizable connector 604 is stopped, the connector valve 640 is closed and the male connector 630 is partially withdrawn from the chambers 632 so that air can enter the disposable fluid line 10 through a recess 642 formed in the wall of the inlet chambers 632. The remaining fluid in the disposable fluid line 10 can then be pumped out to drain the disposable dialysate line 10, as indicated by the arrows in Figure 19d.

[0411] Referring back to Figure 7, from the ~~sterilisable~~sterilizable connector 604, the PD fluid passes out of the patient fill connection 9a through the disposable fluid line 10 to the patient's peritoneal cavity. Patient pinch valves 624, which open and close together, are provided on the patient fill connection 9a and the patient drain connection 9b to allow the machine to physically stop the flow of PD fluid in an emergency by pinching the disposable fluid line 10 between two jaws (not shown) which are normally closed. The pinch valves 624 are only opened by the control system and the protective system if it is sure that the

apparatus is operating correctly and it is safe to deliver PD fluid to the patient.

[0412] The pinch valves are also opened during insertion of the disposable line set before use.

[0413] Figure 20 shows the disposable fluid line 10 for connection to the ~~sterilizable~~sterilizable connector 604. From the male connector 630, two separate tubes 644 extend to a Y-connector 646. The Y-connector 646 connects the two pipes 644 to a standard catheter connector 654 via a manual pinch valve 648. The catheter connector 654 is the only patient connection in the whole apparatus 100 which is not machine ~~sterilized~~sterilized. In contrast, traditional PD treatment systems include several aseptic connections which may introduce potentially harmful bacteria into the peritoneal cavity and lead to peritonitis. Because the apparatus includes only one aseptic connection, the risk of peritonitis is significantly reduced. The only aseptic connection may be replaced by a sterile connection, for example a connection performed by a sterile welding device, cutting a portion of the end of the line set 10 and a portion of a patient tube with a hot wafer and immediately joining the hot ends to obtain a sterile connection. The patient tube is partially consumed and need to be replaced with certain intervals. This technique is well known and used. Another connection technique claimed to be sterile is a connector ~~sterilized~~sterilized by ultraviolet light during the connection cycle.

[0414] The distance between the Y-connector 646 and the catheter connector 654 is kept as small as possible so that the dead space in the disposable fluid line 10 is small, such as less than 2 ml. The pressure drop in one direction across the disposable fluid line 10 is small, such as less than 40 mbar (4 kPa) at a flow rate of 300 ml/min.

[0415] Figure 21 shows an alternative version of the disposable dialysate line 10a, which is used when a sample of the patient's dialysate is to be collected. The sampling disposable dialysate line 10a comprises, in addition to the

features of the normal disposable dialysate line 10, a syringe 652 which fits into a drive mechanism (not shown) in the sampling module 700. The syringe 652 draws off 15 ml of the drained dialysate. Since the dialysate is mixed within the body, the sampling may take place any time during the drain cycle and will represents an average of the whole treatment session. The filled syringe 652 can then be broken off from the sampling disposable dialysate line 10a by means of a self-sealing frangible connection (not shown) and sent for analysis. If desired, the syringe can be visually examined to check the clarity of the dialysate.

[0416] Referring back to Figure 7, when it is desired to empty the patient's peritoneal cavity, the drained fluid is drawn through the disposable fluid line 10 to the patient drain connection 9b, through the ~~sterilisable~~sterilizable connector 604, and then through a patient drain cut-off valve 606. From the patient drain cut-off valve 606 the drained fluid passes through a first patient drain valve 608 and past two independent patient drain pressure sensors 610, which monitor that the negative pressure applied to the peritoneal cavity of the patient by the negative pressure drain connection 14a is not so great as to harm the patient. Downstream of the patient drain pressure sensors 610 the output volumetric flow meter 650 measures the volume of fluid removed from the patient's peritoneal cavity, and a second patient drain valve 612 is provided downstream of the volumetric flow meter 650 to close off the negative pressure drain connection 14a.

[0417] A ~~sterilisation~~sterilization bypass valve 614 allows a fluid path to be opened from the sterile fluid connection 8a to the negative pressure drain connection 14a without going through the patient, when a patient bypass valve 616 is open. The PD fluid can be directed directly to the ambient pressure drain connection 14b, without passing through the patient, by opening a ~~sterilisation~~sterilization heat recovery bypass valve 618 downstream of the patient bypass valve 616.

[0418] During filling of the patient, the pressure of the PD fluid entering the peritoneal cavity is monitored by closing the patient bypass valve 616, the ~~sterilisation~~sterilization bypass valve 614 and the second patient drain valve 612, and opening the first patient drain valve 608 and the patient drain cut-off valve 606. In this way the pressure at the patient's peritoneal cavity is transmitted back from the Y-connector 646 of the disposable fluid line 10 ~~via~~by means of the patient pinch valve 624, the patient drain cut-off valve 606 and the first patient drain valve 608 to the patient drain pressure sensors 610, although there is no flow along this fluid path because the second patient drain valve 612 is closed. By means of this arrangement, the patient drain pressure sensors 610 can measure accurately the pressure of the fluid entering the patient's peritoneal cavity during filling thereof, because the pressure measurement is made as close to the peritoneal cavity as possible.

[0419] The pressure sensors 610 may control the drain pump 508 to start operation (and opening of valve 612) if the positive pressure becomes too large, such as more than 2 meter water pillar over atmosphere pressure, to thereby shunt a portion of the fill fluid to the waste.

[0420] A pressure conditioning chamber 660 similar to pressure conditioning chamber 510 may be provided after patient fill valve 602 as shown by broken lines in Fig 7. The operation of chamber 660 is the same as described for chamber 510.

[0421] Alternatively, the patient drain cut-off valve 606 can be closed and the patient bypass valve 616 and the ~~sterilisation~~sterilization bypass valve 614 can be opened, with the ~~sterilisation~~sterilization heat recovery bypass valve 618 closed. In this way, a pressure tap from the sterile fluid connection 8a to the patient drain pressure sensors 610 is formed, such that the patient drain pressure sensors 610 can measure the pressure of the fluid entering the peritoneal cavity of the patient along the sterile fluid connection 8a.

[0422] Monitoring of the pressure at the peritoneal cavity, enables the control system to detect whether the patient has blocked or disconnected the disposable dialysate line 10.

[0423] During ~~sterilisation~~sterilization of the ~~sterilisable~~sterilizable connector 604, hot ~~sterilising~~sterilizing fluid enters the cyclor and ~~sterilisable~~sterilizable connector module 600 under pressure through the sterile fluid connection 8a and passes through the patient fluid valve 602, through the ~~sterilisable~~sterilizable connector 604, through the patient drain cut-off valve 606, and through the ~~sterilisation~~sterilization bypass valve 614 to the ~~sterilisation~~sterilization output connection 8b. The first patient drain valve 608 is closed during ~~sterilisation~~sterilization to prevent the ~~sterilising~~sterilizing fluid reaching the output volumetric ~~flowmeter~~flow meter 650, which may be damaged at the ~~sterilisation~~sterilization temperature, and also to prevent the patient drain pressure sensors 610 from being subjected to the high pressure required to stop the water at ~~sterilisation~~sterilization temperature from boiling. Flow meters and pressure sensors that have the necessary accuracy for this role and can withstand the ~~sterilisation~~sterilization pressure and temperature are expensive. Thus, the provision of the first patient drain valve 608 reduces the cost of the apparatus 100.

[0424] The heat from the ~~sterilising~~sterilizing fluid is recovered in the thermal control and ~~sterilisation~~sterilization module 300 and the cooled fluid is returned to the cyclor and ~~sterilisable~~sterilizable connector module 600 through the ~~sterilisation~~sterilization fluid return connection 8c. The fluid passes to the ambient pressure drain connection 14b through a ~~sterilisation~~sterilization pressure release valve 620 to return the fluid to ambient pressure and through a ~~sterilisation~~sterilization return shut-off valve 622.

[0425] In a second ~~sterilisation~~sterilization route, the

patient fill valve 602 is closed and the patient bypass valve 616 is opened so that ~~sterilisation~~sterilization fluid at high temperature and pressure can pass from the sterile fluid connection 8a to the ~~sterilisation~~sterilization output connection 8b via the patient bypass valve 616.

[0426] For disinfection, fluid at disinfection temperature is passed through the fluid lines of the cyclor and ~~sterilisable~~sterilizable connector module 600 and out through the negative pressure drain connection 14a and the ambient pressure drain connection 14b, to disinfect those components which are not ~~sterilise~~sterilized.

[0427] Operation of the apparatus

[0428] The operation of the apparatus 100 as a whole will now be described. The default state of all valves is closed for most of the valves. Thus, in its initial operating mode, the inlet valve 202 of the water preparation module 200 and the thermal drain connection valve 520 and the heat recovery return valve 532 of the drainage module 500 are closed, as are the patient pinch valves 624 of the cyclor and ~~sterilisable~~sterilizable connector module 600. In this state therefore the apparatus is sealed off from the external environment.

[0429] Initially, the concentrate disposable container 402 is not connected to the manifold 404, but the disposable fluid line 10 (with membranes 634 intact) is partially inserted in the ~~sterilisable~~sterilizable connector 604. All of the pumps and heaters of the apparatus are initially inoperative, and the patient output heat exchanger 314 is initially drained of water.

[0430] Disinfection of the apparatus

[0431] The first stage of operation is the disinfection of the entire fluid circuit, starting with the water preparation module 200. For disinfection, the inlet valve 202 is opened so that water can flow into the isolator 208. The isolator air vent valve 209 is open to allow air from the isolator 208 to exit to atmosphere through the isolator air vent 17. The

disinfectant selection valve 256 is positioned to direct the waste flow from the second RO membrane unit 252 through the disinfectant cartridge 210 and through the disinfection valve 212, which is open. The degassing pump 222 is operative and draws fluid through the disinfection cartridge 210, or from the isolator 208 if insufficient fluid is available from the fluid path through the disinfection cartridge 210. The fluid from the disinfection cartridge 210 (or the isolator 208) passes to the thermal control and ~~sterilisation~~sterilization module 300 via the cooling water output 2a and is preheated by the water heater 322 before being returned to the water preparation module 200 via the cooling water return connection 2b. The fluid then passes through the degassing components, 214- through 224, which degas the fluid.

[0432] The RO pump 236 is operative to draw fluid from the degassing chamber 224 and pass the fluid through the first RO membrane unit 238. The first RO membrane bypass valve 250 is open so that waste fluid from the first RO membrane unit 238 is redirected to the output side of the RO membrane to continue the fluid path. No fluid from the first RO membrane unit 238 passes through the purification waste connection 2d, because the flow path through this connection is stopped by the thermal drain connection valve 520 in the drainage module 500. Disinfection fluid from the output side of the first RO membrane unit 238 passes through the RO pressure relief valve 260 and also past the second RO membrane unit 252 and is recirculated back to the disinfectant selection valve 256. Thus, it will be seen that a first disinfection loop is provided according to which water is circulated through the disinfection cartridge 210 to dilute the disinfectant and the diluted disinfectant is circulated through the majority of the water preparation module 200. None of the pumps in the thermal control and ~~sterilisation~~sterilization module 300, the concentrate mixing module 400 or the drainage module 500 are operative during the initial disinfection of the water preparation module 200. There are therefore no components that

pump fluid from the purified water connection 2c, such that a negligible amount of fluid crosses the second RO membrane unit 252 because there is no pressure differential across the membrane unit 252. Any fluid which does cross the second RO membrane unit 252 is routed to the external drain connection via the purified water connection 2c, the mixing water feed connection 4a, the mixing system bypass valve 440, the mixing module output connection 4b, the OLA input valve 356, the sterile fluid connection 8a, the patient bypass valve 616, the ~~sterilisation~~sterilization heat recovery bypass valve 618, the ambient pressure drain connection 14b, the heat recovery drain connection 13b, the heat recovery drain return connection 13c and the open heat recovery return valve 532. This water is replaced by water from the tap water inlet 1 ~~via~~by means of particle filter 204 and water softener 206.

[0433] During the first phase of disinfection of the water preparation module 200, the air bleed valve 320 in the thermal control and ~~sterilisation~~sterilization module 300 is opened and the patient output heat exchanger pump 316 is operated to fill the patient output heat exchanger with disinfectant and to recirculate this disinfectant through the recirculation restrictor 310.

[0434] By closing the proportioning valve 214 completely with the degassing bypass valve 226 also closed, the flow through the cooling water return connection 2b is stopped. The patient output heat exchanger pump 316 is then used to pump disinfectant from the cooling water output 2a through the open air bleed valve 320, through the patient output heat exchanger vent connection 2e and into the isolator 208 to disinfect the patient output heat exchanger vent connection 2e. The isolator air vent valve 209 is closed during this process. The disinfectant from the isolator 208 continues to the cooling water output 2a of the water preparation module 200 to close this disinfectant circulation loop.

[0435] The patient output heat exchanger 314 can be drained of disinfectant by subsequently opening the isolator air vent

valve 209 and the air bleed valve 320 while the patient output heat exchanger drain valve 318 is open and fluid is circulating between the cooling water output 2a and the cooling water return connection 2b when the patient output heat exchanger pump 316 is inoperative.

[0436] The air passage between the degassing chamber 224 and the isolator 208 is disinfected by closing the isolator air vent valve 209 and opening the degassing bypass valve 226. The degassing pump 222 is then operated with the RO pump 236 off such that the only flow from the degassing chamber 224 is directly to the isolator 208 through the air passage.

[0437] At the end of the disinfection process, the disinfectant selector valve 256 is returned to its default position with the first RO membrane bypass valve 250 still open. Disinfectant is circulated by the RO pump 236 past the first RO membrane unit 238, the second RO membrane unit 252 and back round to the RO pump 236 via the second RO output restrictor 254 and the disinfectant selection valve 256. After this circulation, the first RO membrane bypass valve 250 is closed and the thermal drain connection valve 520 in the drainage module 500 is opened so that disinfectant can flow through the purification waste connection 2d to the thermal drain connection 13a and out of the external drain connection 16.

[0438] Finally, the water preparation module 200 is flushed with water to remove any remaining disinfectant along the disinfectant routes described above.

[0439] It will be seen from the above that the entire water preparation module 200 from the water softener 206 up to and including the second RO membrane unit 252 is chemically disinfected by the above process.

[0440] Downstream of the second RO membrane unit 252, water at disinfection temperature supplied from the RO membrane disinfection connection 3 is used to disinfect the fluid path between the second RO membrane unit 252 and the purified water connection 2c. In this case, water from the tap water

connection 1 passes along the normal purification fluid path through the water preparation module 200 so that RO water is produced at the output side of the second RO membrane unit 252. The mixing water stop valve 442 of the concentrate mixing module 400 is opened and the salt input displacement pump 452 is energised to draw water from the mixing water feed connection 4a. The water supply to the mixing water feed connection 4a of the mixing module 400 is drawn from the purified water connection 2c of the water preparation module 200 and heated to disinfection temperature by the disinfection heater 330. The salt input displacement pump 452 pumps the water at disinfection temperature through the open RO membrane disinfection valve 499 to the output side of the second RO membrane unit 252 via-by means of the RO membrane disinfection connection 3. Thus, a closed recirculation loop of water at disinfection temperature is provided, the temperature of which is monitored by the second RO temperature sensor 264.

[0441] The disinfection heat exchanger bypass valve 328 is disinfected as part of the above heat disinfection loop, by opening the valve to allow the hot disinfection water to pass there through.

[0442] The hot water is flushed to the drainage module 500 by deactivating the salt input displacement pump 452 and activating the flow control pump 446 to pump the hot water to the drainage module 500 via the mixing module drain connection 15.

[0443] Before the disposable concentrate container 402 is connected to the manifold 404, the manifold 404 and cap 406 are heat disinfected. To achieve this, the cap 406 is located on the manifold 404 to form a sealed cavity. The flow control pump 446 is activated to pump water heated to disinfection temperature by the disinfection heater 330 through the mixing water feed connection 4a. The flow control pump 446 pumps the disinfection water through the reservoir filling valve 466 and into the concentrate reservoir 468. The hot disinfecting fluid is pumped into the cavity formed by the manifold 404 and cap

406 sequentially in time through each of the reservoir vent disinfection valve 498, the reservoir output valve 470 and each of the salt input valves, 478- through 488, so that all of these valves are disinfected. The cap air vent valve 474 vents air from the cavity formed by the manifold 404 and the cap 406 to the drainage module 500 via the mixing module drain connection 15. Once the manifold 404 and cap 406 are full of hot disinfection fluid, the fluid is forced through the mixing module drain connection 15 via-by means of the cap air vent valve 474 to the drainage module 500.

[0444] In the drainage module 500, the hot fluid passes out of the heat recovery drain connection 13b and through the disinfection heat exchanger 326. However, the disinfection heat exchanger bypass valve 328 is open so that no heat is lost from the disinfection fluid passing through the disinfection heat exchanger 326 and returning to the drainage module 500 via-by means of the heat recovery drain return connection 13c. In this way, the heat recovery drain connection 13b and the heat recovery return valve 532 are also heat disinfected.

[0445] In order to disinfect the sodium bicarbonate air vent valve 492, water at disinfection temperature from the thermal control and ~~sterilisation~~sterilization module 300 is drawn via-through the mixing water feed connection 4a by the salt input displacement pump 452. At this time, the only open fluid passages into the filled cavity formed by the manifold 404 and the cap 406 are via-by means of the sodium bicarbonate air vent valve 492 and the sodium bicarbonate input valve 482. Thus, as the salt input displacement pump 452 pumps hot water out of the cavity formed by the manifold 404 and the cap 406 via the sodium bicarbonate input valve 482 the hot water is replaced from the mixing water feed connection 4a via-by means of the sodium bicarbonate air vent valve 492. The sodium bicarbonate air vent valve 492 is toggled to disinfect the air vent and the fluid channel 428. The hot water is recirculated through this loop by closing the heat recovery return valve

532 in the drainage module 500 and opening the mixing water stop valve 442. The same method can be used to disinfect the sodium chloride air vent valve 494 and the sodium chloride input valve 484.

[0446] The fluid path to the glucose compartment 420 of the disposable concentrate container 402 is disinfected by using the flow control pump 446 to pump hot water from the thermal control and ~~sterilisation~~sterilization module 300 ~~via-by means of~~ the mixing water feed connection 4a through the mixing system bypass valve 440, the glucose selector valve 444 and the glucose input valve 490 into the cavity formed by the manifold 404 and the cap 406. Subsequently, with the flow control pump 446 switched off, the glucose recirculation pump 448 is used to recirculate the hot water through the glucose output channel 436 and the fluid input channel 434. The glucose input valve 490 is closed at this stage. Finally, the hot disinfection fluid can exit the cavity formed by the manifold 404 and cap 406 via the cap air vent valve 474 and the mixing module drain connection 15.

[0447] After disinfection, the manifold 404 and cap 406 are drained by connecting the cavity formed thereby to atmosphere at the air vent 6 by means of the cap air vent valve 474, and pumping the water out of the manifold and cap 406 using the salt input displacement pump 452 ~~via-by means of~~ the reservoir vent disinfection valve 498, the concentrate reservoir 468 and the reservoir output valve 470. The salt input displacement pump 452 pumps the water to the drainage module ~~via-by means of~~ the flow control pump bypass valve 458, the drain disinfection valve 464 and the mixing module drain connection 15.

[0448] In order to disinfect the thermal control and ~~sterilisation~~sterilization module 300 and the cycler and ~~sterilisable~~sterilizable connector module 600, hot water is pumped by the volumetric pump 352 from the disinfection heater 330 ~~via-by means of~~ the mixing water feed connection 4a, the mixing system bypass valve 440 and the mixing module output

connection 4b through the OLA input valve 356. In a further route, the disinfection fluid is pumped through the OLA ~~sterilisation~~sterilization valve 376. The disinfection fluid passes through the thermal control and ~~sterilisation~~sterilization module 300 to the sterile fluid connection 8a and then through the patient fill valve 602, through the chamber 632 and fluid passage 640 of the ~~sterilisable~~sterilizable connector 604, the patient drain cut-off valve 606, the ~~sterilisation~~sterilization bypass valve 614 the ~~sterilisation~~sterilization heat recovery bypass valve 618 and into the drainage module 500 ~~via~~ by means of the ambient pressure drain connection 14b.

[0449] In a further disinfection route, the disinfection fluid entering the cyclor and ~~sterilisable~~sterilizable connector module 600 through the sterile fluid connection 8a, passes through the patient bypass valve 616, and through the ~~sterilisation~~sterilization heat exchanger 378 via the ~~sterilisation~~sterilization output connection 8b. At this time, there is no fluid flow through the other side of the ~~sterilisation~~sterilization heat exchanger 378 and thus no heat is lost from the disinfection fluid during its passage through the ~~sterilisation~~sterilization heat exchanger 378. The disinfection fluid entering the cyclor and ~~sterilisable~~sterilizable connector module 600 via the ~~sterilisation~~sterilization fluid return connection 8c passes to the drainage module 500 via the ambient pressure drain connection 14b.

[0450] In the final disinfection route through the cyclor and ~~sterilisable~~sterilizable connector module 600, hot disinfection fluid from the sterile fluid connection 8a passes through the patient fill valve 602, the ~~sterilisable~~sterilizable connector 604, the patient drain cut-off valve 606, the first patient drain valve 608 and onward to the negative pressure drain connection 14a. At this time, the drainage pump 508 is operative.

[0451] It will be seen from the above that the whole fluid

system from the water softener 206 to the patient pinch valves 624, including the drainage module 500 can be disinfected either chemically or by heat disinfection.

[0452] Cleaning and Flushing

[0453] After disinfection, the disposable concentrate container 402 is connected to the manifold 404, and a downstream cleaning operation is then carried out.

[0454] For the cleaning operation, RO water preheated by the disinfection heater 330 to mixing temperature is drawn into the concentrate mixing module 400 by the salt input displacement pump 452 ~~via~~through the mixing water stop valve 442 and directed through the cleaning agent input valve 480 into the cleaning agent compartment 410 of the concentrate disposable container 402. Sufficient water is pumped into the cleaning agent compartment 410 to dissolve all of the powdered cleaning agent stored therein. Once the cleaning agent is dissolved, the salt input displacement pump 452 is reversed to draw the cleaning agent solution out of the cleaning agent compartment 410 through the cleaning agent input valve 480. The cleaning agent is pumped into the concentrate reservoir 468 via the reservoir filling valve 466 by the salt input displacement pump 452. From the concentrate reservoir 468, the cleaning agent is passed to the drainage module 500 via the reservoir air vent valve 496 and the mixing module drain connection 15.

[0455] For cleaning of the downstream components in the thermal control and ~~sterilisation~~sterilization module 300 and the cyclor and ~~sterilisable~~sterilizable connector module 600, the cleaning agent is pumped by the salt input displacement pump 452 through the flow control pump bypass valve 458 and the reservoir filling valve 466 to the mixing module output connection 4b. The flow of cleaning agent is directed through the thermal control and ~~sterilisation~~sterilization module 300 and the cyclor and ~~sterilisable~~sterilizable connector module 600 according to any of the disinfection routes described above.

[0456] After cleaning, the thermal control and ~~sterilisation~~sterilization module 300 and the cycler and ~~sterilisable~~sterilizable connector module 600 are flushed with purified water from the water preparation module 200 to remove any remaining cleaning agent.

[0457] The cleaning agent may be sodium carbonate, but other cleaning agents may be used, such as citric acid, or precursors for a cleaning agent.

[0458] Treatment

[0459] Once the fluid system has been disinfected, cleaned and flushed, the first stage of the treatment process is the dissolution of the salts and glucose in the concentrate disposable container 402. Thus, RO water at mixing temperature is pumped by the salt input displacement pump 452 through the mixing water stop valve 442 sequentially into each of the salt compartments, 412- through 418, through the respective input valves, 482- through 488. Sufficient water is pumped by the salt input displacement pump 452 to fill the respective compartment, 412- through 418, of the concentrate disposable container 402, but the volume of fluid pumped by the salt input displacement pump 452 is carefully monitored to ensure that too much water is not input into the compartment, 412- through 418, which would overflow through the air vent channel, 424- and 428. Once each compartment, 412- through 418, is full, the respective input valve, 482- through 488, is closed while the salt dissolves. The volumes of water input into the compartments, 408- and 412- through 418, are carefully selected. Thus, the control system knows how much water is in each compartment. If too much water is introduced into the sodium bicarbonate 412 or the sodium chloride compartment 414 no harm is done because the resultant solution will still be substantially saturated.

[0460] For filling of the glucose compartment 420, RO water at mixing temperature, for example 37°C, is pumped by the flow control pump 446 from the mixing water feed connection 4a via by means of the mixing system bypass valve 440, the reservoir

filling valve 466 and the glucose selector valve 444 through the open glucose input valve 490 into the glucose compartment 420 ~~via~~ by means of the fluid input channel 434. The glucose recirculation pump 448 is deactivated at this stage. Once sufficient fluid has been pumped into the glucose compartment 420 to fill that compartment to a level not exceeding the top of the glucose air vent channel 432, the glucose input valve 490 is closed and the glucose recirculation pump 448 recirculates the glucose solution to aid dissolution. The volume of water pumped into the glucose compartment 420 determines the concentration of the glucose solution.

[0461] While the glucose and salts are dissolving, the patient fluid circuit is ~~sterilise~~ sterilized. Thus, RO water is drawn by the volumetric pump 352 from the mixing water feed connection 4a through the mixing system bypass valve 440 and the mixing module output connection 4b and is pumped through the OLA ~~sterilisation~~ sterilization valve 376. The water passes through the ~~sterilisation~~ sterilization heat exchanger 378, where it is preheated, and then through the second OLA heat exchanger 362 for further preheating. The volumetric pump 352 pressurises the water to a sufficiently high pressure that the OLA heating bath 364 can raise the temperature of the water to a suitable ~~sterilisation~~ sterilization temperature, i.e. above 100°C, preferably above 121°C, without boiling. The heated pressurised water passes through the hot side of the second OLA heat exchanger 362 and of the first OLA heat exchanger 360. However, because there is no flow through the cold side of the first OLA heat exchanger 360, no heat is transferred from the heated pressurised water. Similarly, as the heated pressurised water passes through the patient output heat exchanger 314, no heat is transferred because the water bath in the patient output heat exchanger 314 has been drained. The heated pressurised water passes through the patient output pressure relief valve 374, which is deactivated so that there is no drop in pressure, and enters the cycler and ~~sterilisable~~ sterilizable connector module 600 via the sterile

fluid connection 8a.

[0462] In the cycler and ~~sterilisable~~sterilizable connector module 600 the heated pressurised water firstly passes through the patient fill valve 602, the ~~sterilisable~~sterilizable connector 604, the patient drain cut-off valve 606 and the ~~sterilisation~~sterilization bypass valve 614 to the ~~sterilisation~~sterilization output connection 8b. The first patient drain valve 608 is closed during this operation to protect the patient drain pressure sensors 610 from the elevated pressure and the output volumetric flow meter 650 from the elevated temperature. Thus, the fluid path between the first patient drain valve 608 and the drainage module 500 is not ~~sterilise~~sterilized. However, this line has been disinfected and does not handle fluid which is subsequently passed to the patient, so that there is no risk to the patient. From the ~~sterilisation~~sterilization output connection 8b the heated pressurised water passes through the ~~sterilisation~~sterilization heat exchanger 378 where its temperature is reduced by heat transfer to the relatively cool water passing through the OLA ~~sterilisation~~sterilization valve 376. The cooled pressurised water then passes via the ~~sterilisation~~sterilization fluid return connection 8c through the ~~sterilisation~~sterilization pressure relief valve 620 which reduces the pressure to atmospheric. The cooled ambient pressure water passes through the ~~sterilisation~~sterilization return shut-off valve 622, through the ambient pressure drain connection 14b and the heat recovery drain connection 13b to the disinfection heat exchanger 326 where the temperature of the water is further reduced before the water is passed to the external waste connection 16 via the heat recovery drain return connection 13c and the heat recovery return valve 532.

[0463] During a further stage of the ~~sterilisation~~sterilization of the cycler and ~~sterilisable~~sterilizable connector module 600 the patient fill valve 602 and the ~~sterilisation~~sterilization bypass valve 614 are closed so that the high temperature pressurised water can

pass through the patient bypass valve 616 (which is now open) to the ~~sterilisation~~sterilization output connection 8b to ~~sterilise~~sterilize the patient bypass valve 616.

[0464] In the above manner, it is ensured that the fluid circuit from the OLA heating bath 364 to the ~~sterilisation~~sterilization heat exchanger 378 is sterile. The sterility is maintained throughout the treatment session.

[0465] Once the fluid path from the OLA 375 to the ~~sterilisable~~sterilizable connector 604 has been ~~sterilise~~sterilized, sterile fluid is passed along this path continuously until the end of the treatment session to maintain sterility. The fluid may be water from the water preparation module 200 which passes from the mixing water feed connection 4a through the mixing system bypass valve 440 to the mixing module output connection 4b, through the OLA 375, where it is ~~sterilise~~sterilized and then through the patient bypass valve 616 and the ~~sterilisation~~sterilization heat recovery bypass valve 618 to the drainage module 500. Alternatively, the fluid may be PD fluid from the concentrate mixing module 400 which is ~~sterilise~~sterilized in the OLA 375 and passed to the drainage module 500 along the same fluid path as described above. In this way, the OLA 375 can operate continuously without overheating to ensure sterility at all times. When the PD fluid is to be delivered to the patient, the patient bypass valve 616 is shut and the patient fill valve 602 is opened to allow the PD fluid to pass to the ~~sterilisable~~sterilizable connector 604.

[0466] Once the ~~sterilisation~~sterilization operation has been completed, the concentrated PD fluid is mixed in the concentrate reservoir 468 in the manner described in detail above in relation to the concentrate mixing module 400.

[0467] While the concentrated PD fluid is being mixed, the water bath of the patient output heat exchanger 314 is filled by opening the air bleed valve 320 and activating the patient output heat exchanger pump 316, in preparation for delivery of PD fluid to the patient.

[0468] The apparatus is now ready for the arrival of the patient. When the patient arrives, the membranes 634 on the disposable fluid line 10 are pierced by the ~~sterilisable~~sterilizable connector 604. The disposable fluid line 10 is primed by pumping PD fluid (or sterile water) from the mixing module output connection 4b through the OLA input valve 356 using the volumetric pump 352. The PD fluid is produced in the mixing module 400 by diluting the concentrated PD fluid pumped by the salt input displacement pump 452 from the concentrate reservoir 468 to the mixing chamber 450 with a flow of purified water from the water preparation module 200. The flow control pump 446 is bypassed during delivery of the PD fluid by opening the flow control pump bypass valve 458. The PD fluid passes through the first OLA heat exchanger 360, the second OLA heat exchanger 362 and the OLA heating bath 364 and is thereby ~~sterilisesterilized~~. The ~~sterilisesterilized~~ PD fluid is brought down to the required patient temperature by the patient output heat exchanger 314 and is depressurised by the patient output pressure relief valve 374. The sterile PD fluid is then passed through the patient fill valve 602 and the patient pinch valve 624 into the disposable dialysate line 10. The PD fluid passes through the disposable fluid line 10 and returns to the sterile connector 604 via the second patient pinch valve 624. The returned fluid passes through the patient drain cut-off valve 606 and the first patient drain valve 608. The output volumetric flow meter 650 registers the fluid flow and confirms that the disposable fluid line 10 has been successfully primed with PD fluid. The PD fluid then passes to the drainage module 500 via the negative pressure drain connection 14a. In this way, it is ensured that there is only a minimal amount of air in the disposable dialysate line which connects to the patient's peritoneal cavity.

[0469] Once the disposable fluid line 10 has been primed, the patient is invited to connect to the disposable fluid line 10 so that any fluid in the patient's peritoneal cavity can be drained. During draining of the patient the drainage pump 508

is activated to draw dialysate from the ~~sterilisable~~sterilizable connector 604 through the patient drain cut-off valve 606 and past the output volumetric flow meter 650 to the negative pressure drain connection 14a. The output volumetric flow meter 650 records the volume of dialysate withdrawn from the patient's cavity. During drainage, a sample of the patient's dialysate may be taken by the sampling module 700.

[0470] In the case of subsequent filling and draining of the patient's cavity, additional concentrated PD fluid is mixed by the mixing module 400 in the concentrate reservoir 468 while the patient is being drained by the cyclor and ~~sterilisable~~sterilizable connector module 600 and the drainage module 500.

[0471] When the patient's peritoneal cavity is empty, which is registered by a drop in pressure or flow rate detected by the patient drain pressure sensor 610 or the output volumetric flow meter 650, or when a predetermined drain time has elapsed, the drainage pump 508 is deactivated. The patient's peritoneal cavity can then be filled with sterile PD fluid from the sterile fluid connection 8a of the thermal control and ~~sterilisation~~sterilization module 300 ~~via~~by means of the patient fill valve 602, the ~~sterilisable~~sterilizable connector 604 and the patient pinch valve 624. During filling of the patient, the pressure of the PD fluid entering the patient is monitored using the pressure tap described in detail above in relation to the cyclor and ~~sterilisable~~sterilizable connector module 600. The volume of PD fluid entering the patient's peritoneal cavity is recorded by the input volumetric flow meter 350.

[0472] Once sufficient fluid has been passed to the patient, the fluid system downstream of the mixing module output connection 4b is flushed through to the drainage module 500 firstly with the remaining PD fluid (which is ~~sterilise~~sterilized) and then with ~~sterilise~~sterilized water to remove any glucose deposits that remain in the OLA 375 and

would caramelise. The system then awaits drainage of the patient. Thus, a cycle of drains and fills can be repeated over an extended period to complete a treatment session.

[0473] At the end of a treatment session, once the patient has disconnected from the apparatus 100, any remaining salt or glucose solutions in the concentrate disposable container 402 are pumped to the drainage module ~~via-by means of~~ the mixing module drain connection 15. The fluid system is then flushed with clean water utilising the disinfection routes described above. The concentrate disposable container 402 and the disposable fluid line 10 are replaced. Finally, the system is cleaned as described above and then flushed with clean water, before the system is shut by closing the inlet valve 202, the thermal drain connection valve 520 and the heat recovery return valve 532. The apparatus is then ready for the next treatment session.

[0474] During extended periods of non-use, the entire fluid system may be filled by an engineer with a suitable preservative and closed to atmosphere to prevent bacteriological build-up.

[0475] It is mentioned that the apparatus has a memory device capable of storing information for later ~~retrival~~ retrieval. Such a memory device may be a hard disk or a solid state memory device. Parameters to be stored in a technical log may be selected from the following non-exhaustive list: time and result of processes, like cleaning, ~~sterilisation~~ sterilization, verification of sterility; flow rates; conditions of valves, pumps; pump speeds; sensor values such as conductivities, temperatures, pressures, temperatures.

[0476] It will be apparent to those skilled in the art that various modifications and variations can be made to the structure and methodology of the present invention without departing from the scope or spirit of the invention. For example, certain aspects of the structure and methodology of the invention which have been particularly described in relation to peritoneal dialysis could be used for acute

dialysis, home dialysis, chronic dialysis in general including hemodialysis or hemofiltration or hemodiafiltration or any other medical fluid production or treatment procedure (including producing nutritional solutions) especially those involving infusion and/or removal of fluids to and/or from a patient. Thus, it should be understood that the present invention is not limited to the examples discussed in this specification and shown in the drawings. Rather, the invention is intended to cover modifications and variations provided they come within the scope of the following claims and their equivalents.

[0477] Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention as defined by the appended claims.

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METHOD, APPARATUS AND COMPONENTS OF DIALYSIS SYSTEMS

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application relies on the benefit of priority Swedish Patent application No. 9901165-2, filed March 30, 1999, the entire disclosure of which is incorporated herein by reference. In addition, related U.S. provisional patent application Serial No. 60/127,179, filed March 30, 1999, is also incorporated herein by reference.

FIELD OF THE INVENTION

[0002] The present invention relates to methods, apparatus and components of dialysis systems, such as peritoneal dialysis, hemodialysis, hemodiafiltration or hemofiltration systems.

BACKGROUND OF THE INVENTION

[0003] Kidney dysfunction is a serious and life-threatening condition wherein the kidneys of a mammal do not function properly to remove impurities, remove excess water and perform other physiologically important activities. A person affected with kidney dysfunction needs to undergo regular dialysis treatments so that the blood can be purified and water removed.

[0004] In one type of conventional dialysis procedure, peritoneal dialysis (PD), a PD fluid is administered to the peritoneal cavity of a mammalian patient to dwell there and later be removed as a spent dialysate. Waste products are transferred to the PD fluid and are removed together with the spent dialysate. An osmotic agent in the PD fluid causes removal of excess water. A buffer in the PD fluid causes replenishment of the body buffer. Further electrolytes are balanced by the PD fluid.

[0005] Because PD fluid is passed into the patient's body there is a risk of infection, which sometimes results in peritonitis.

[0006] For performing peritoneal dialysis, couplings are used for connecting a catheter ending in a peritoneal cavity to a source of PD fluid. In an attempt to reduce patient

infection, such couplings are made as "aseptic" or "sterile" couplings. Although aseptic couplings aid in reducing the contamination of PD fluid, each coupling may permit entry of potentially harmful microorganisms, such as bacteria and fungi, into an otherwise sterile PD system, and, eventually, being transfer to the peritoneal cavity. Reducing the number of these couplings may reduce the risk of infection and peritonitis.

[0007] Traditionally, sterile PD fluid is stored in, and administered to a patient from a plastic fluid bag. An aseptic coupling is typically used to connect the fluid bags to the catheter of the patient. Each coupling increases the chances of bacterial and other contamination.

[0008] The two most common forms of PD, namely, continuous ambulatory peritoneal dialysis (CAPD) and automatic peritoneal dialysis (APD), require many fluid bags to be used per year. CAPD normally relies on gravity to fill and drain PD fluid originating in a bag set and provides continuous treatment while the patient is still relatively free to move. Fluid exchanges are normally performed during the daytime. APD relies on the use of a cycler for pumping PD fluid from fluid bags to perform patient fill and drain cycles, usually overnight, while the patient is asleep. In both cases, a particular prescription of PD fluid is manufactured and packaged in one or more bags under sterile conditions at a production plant, and the bags are then shipped to a patient or physician.

[0009] However, the use of PD fluid bags has a number of drawbacks and disadvantages. Every patient has different dialysis requirements, and those requirements may be different at different times, and therefore benefits from use of a PD fluid that specifically meets the patient's needs. As a result, manufacturers of PD fluid have to make and deliver many different formulations of PD fluid. This often requires storage of a significant number of bags containing different PD fluid formulations in the home of a patient.

[0010] Clinical testing is being performed today using bicarbonate as a buffer instead of conventional lactate buffered PD fluid. Conventional PD fluids have a relatively low pH, which may cause discomfort and even pain during the fill phase. By using bicarbonate as a buffer, PD fluids having a physiological pH may be formulated. However, over time, calcium carbonate, formed from components of the PD fluid, may precipitate out of the solution of the PD fluid, rendering the solution unusable.

[0011] Glucose, another component of PD fluid, may degrade over time particularly when the PD fluid has been subject to conventional heat sterilization in an autoclave. The degradation of glucose may produce degradation products which are potentially harmful to the patient, at least in the long term.

[0012] PD fluid bags are often shipped a significant distance from the point of manufacture to the point of use. Since a large proportion of PD fluid is water, this effectively amounts to transporting large quantities of water from PD fluid production plants to treatment locations, such as hospitals, clinics or patients' homes.

[0013] Further, the size of PD fluid bags is limited because they must be sufficiently lightweight to permit easy handling by a patient or physician. Most PD fluid bags for CAPD contain a relatively small amount of fluid, for example between 0.5 and 5 liters. When higher volumes are required, such as in APD, multiple PD fluid bags may be used during each treatment session. Having more than one PD fluid bag, however, necessitates an aseptic coupling for each bag and requires relatively complicated connection and disconnection procedures when changing bags. These additional connection and disconnection procedures, although aseptic, provide an opportunity for potentially harmful bacteria to enter the dialysis system and cause peritonitis. Four or five connections may be involved in APD.

[0014] In dialysis, specifically acute hemodialysis, bags

of sterile dialysis solution are used. During hemofiltration and hemodiafiltration, infusion solutions are used for infusion into the blood. Such solutions have the same problems as outlined above.

[0015] In U.S. Patent No. 4,718,890, U.S. Patent No. 4,747,822, U.S. Patent No. 5,004,459 and U.S. Patent No. 5,643,201, it has been proposed to make up and administer PD fluid at a treatment location. However, these proposed approaches have various drawbacks and disadvantages. U.S. Patent No. 5,643,201 is illustrative. It discloses a system for preparation of PD fluid, using a concentrated dialysis liquid source as a starting point. In the system, water is purified in a reverse osmosis unit and is then mixed by a volumetric proportioning pump with the liquid concentrate. Additional dextrose solution may be added by a dextrose pump. The mixed fluid is heated to a temperature of 70°C to 80°C and is then cooled to a proper patient temperature, passed to a reservoir where it is weighed to check the amount, and then delivered to the peritoneal cavity of the patient. Since this system uses a concentrated solution as the PD fluid concentrate, there may be problems due to the stability of the concentrates, for example if bicarbonate buffer is used. In addition, the proposed temperature of 70°C to 80°C may not be adequate to achieve a sufficiently high level of sterilization.

[0016] Further, although there is an option of adding additional dextrose, the relative concentrations of the electrolyte components of the PD fluid are fixed by their relative concentrations in their initially concentrated form. Thus, the basic formulation of the PD fluid, apart from the dextrose concentration, is predetermined in advance by the proportions of the constituent substances in the initial concentrated dialysis liquid source. If the system were to be useable with different prescriptions, it would be necessary to provide a range of different concentrated dialysis liquid sources each having the constituent substances present in the

appropriate proportions for that prescription. Thus, a range of sources, such as bags of concentrated dialysis liquid, would be required, leading essentially to the same logistic problem as in the PD treatment systems where the PD fluid is entirely pre-prepared at a remote point of manufacture.

[0017] Another proposal for making aqueous solutions for medical purposes, including PD fluid, is disclosed in British Patent No. 1,450,030. This also uses a concentrated solution as a starting point. Relative concentrations of electrolyte are predetermined by the starting concentrated solution. This proposal from 1972 does not provide detail on how the PD fluid would be delivered to a patient.

[0018] In light of the foregoing, there is a need in the art for improving peritoneal dialysis techniques.

SUMMARY OF THE INVENTION

[0019] In accordance with the present invention, these and other objects have now been realized by the invention of a container for use in the preparation of a peritoneal dialysis fluid, the container comprising a plurality of chambers, and a corresponding plurality of concentrates for the peritoneal dialysis fluid, at least one of the plurality of concentrates in at least one of the chambers comprising a concentrate in the form of a powder.

[0020] In accordance with one embodiment of the present invention, a container is provided for use in the preparation of a dialysis fluid, the container comprises a plurality of chambers, a cleaning agent disposed in at least one of the plurality of chambers, and a powdered inorganic salt disposed in at least one other of the plurality of chambers.

[0021] In accordance with another embodiment of the present invention, a container is provided for use in the preparation of a dialysis fluid, the container comprising a plurality of chambers, a first amount of a first inorganic salt disposed in at least one of the plurality of chambers, and a second amount of a second inorganic salt different from the first inorganic salt disposed in another of the plurality of chambers, the at

least one of the plurality of chambers having a first volume and the another of the plurality of chambers having a second volume, whereby when the first and second inorganic salts are prepared by filling the at least one and the another of the plurality of chambers with a liquid to provide solutions of first and second inorganic salts, the solutions of the first and second inorganic salts have characteristically different conductivities.

[0022] In accordance with another embodiment of the present invention, a container is provided for use in the preparation of a dialysis fluid, the container comprising a plurality of distinct chambers, a corresponding plurality of concentrate components of the dialysis fluid in the plurality of distinct chambers, and a corresponding plurality of connectors for each of the plurality of distinct chambers, each of the plurality of connectors including at least two separate fluid channels so as to provide for simultaneous inflow and outflow from each of the plurality of distinct chambers.

[0023] In accordance with yet another embodiment of the container of the present invention, the container is used for priming powdered glucose at a predetermined patient location, the container including an upper region and a lower region, the powdered glucose, an inlet port in the lower region for receiving a supply of water to dissolve the powdered glucose, and a diffuser associated with the inlet port for diffusing the flow of water into the powdered glucose.

[0024] In accordance with another embodiment of the container of the present invention, the container is used in connection with a dialysis fluid, the container comprising a plurality of distinct chambers, and a corresponding plurality of connectors for each of the plurality of distinct chambers, each of the plurality of connectors being aligned along a predetermined linear axis.

[0025] In accordance with another embodiment of the container of the present invention, the container comprises a universal container for use in connection with a dialysis

solution, the universal container including a plurality of compartments, a corresponding plurality of predetermined amounts of chemical components in each of the plurality of compartments, wherein upon combination with a liquid the plurality of chemical components can provide a plurality of different formulations of the dialysis solution for a corresponding plurality of patient requirements, and at least one port associated with the plurality of compartments for providing fluid communication with a dialysis treatment system.

[0026] In accordance with another embodiment of the container of the present invention, a container is provided for use in the preparation of a dialysis fluid, the container including a first compartment, calcium chloride in the first compartment, a second compartment, magnesium chloride in the second compartment, a third compartment, sodium chloride in the third compartment, a fourth compartment, a cleaning agent in the fourth compartment, a fifth compartment, sodium bicarbonate in the fifth compartment, a sixth compartment, glucose in the sixth compartment, a plurality of ports associated with each of the first, second, third, fourth, fifth and sixth compartments whereby the plurality of ports can be connected to a dialysis treatment unit for preparation of the dialysis solution at a patient treatment location.

[0027] In accordance with another embodiment of the container of the present invention, a container is provided for use in connection with dialysis comprising a plurality of compartments including a first compartment, an ionic component of a dialysis solution disposed in the first compartment, a second compartment, and a cleaning agent or a precursor of the cleaning agent for cleaning a flow path in a dialysis system disposed in the second compartment, the container including a plurality of ports whereby the first and second compartments can be placed in fluid communication with the dialysis system.

[0028] In accordance with another embodiment of the container of the present invention, the container includes a

surface having a longitudinal axis for use in connection with dialysis comprising a plurality of compartments, a corresponding plurality of chemical compositions in each of the plurality of compartments, and a plurality of fluid ports in fluid communication with each of the plurality of compartments, whereby each of the plurality of compartments can be placed in fluid communication with a dialysis system, at least one of the plurality of ports being disposed along the surface of the container asymmetrically with respect to the longitudinal axis of the surface of the container.

[0029] In accordance with another embodiment of the container of the present invention, a container is provided for use in connection with dialysis including a plurality of compartments, a corresponding plurality of chemical components in each of the plurality of compartments, a plurality of ports associated with each of the plurality of compartments for fluid communication with a dialysis system, and readable indicia disposed on the container, the readable indicia being indicative of the contents of the plurality of compartments, whereby the readable indicia can be recognized by the dialysis system.

[0030] In accordance with another embodiment of the container of the present invention, a container is provided for use in connection with dialysis comprising a first compartment including a first air vent channel, a first fluid channel and a first port in fluid communication with the first air vent channel and the first fluid channel, a second compartment including a second air vent channel, a second fluid channel, and a second port in fluid communication with the second air vent channel and the second fluid channel, a third compartment including a third air vent channel, a third fluid channel, and a third port in fluid communication with the third air vent channel and the third fluid channel, a fourth compartment including a fourth air vent channel, a first fourth port in fluid communication with the fourth air vent channel, a fluid input channel, and a diffuser in fluid

communication with the fluid input channel, a fluid output channel, a second fourth port in fluid communication with the fluid input channel and the fluid output channel, and a glucose filter in fluid communication with the fluid output channel, a fifth compartment including a fifth air vent channel, a fifth fluid channel, and a fifth port in fluid communication with the fifth air vent channel and the fifth fluid channel, a sixth compartment including a first air vent/fluid flow channel, a first fluid input/output channel and a sixth port in fluid communication with the first air vent/fluid flow channel and the first fluid input/output channel, a seventh compartment including a second air vent/fluid flow channel, a second fluid input/output channel, and a seventh port in fluid communication with the second air vent/fluid flow channel and the second fluid input/output channel, the plurality of compartments being sized to contain respective amounts of the components of the dialysis solution, the ports being placeable in fluid communication with a dialysis processing machine.

[0031] In accordance with the present invention, apparatus is also provided for the production of peritoneal dialysis solution comprising a plurality of chambers, a corresponding plurality of concentrates of constituents of the peritoneal dialysis solution, a mixer for mixing the corresponding plurality of concentrates with a predetermined liquid to produce the peritoneal dialysis solution, a sterilizer for sterilizing at least one of the peritoneal dialysis solution and the predetermined liquid, and a patient connector for supplying the peritoneal dialysis solution to the peritoneal cavity of the patient, at least one of the corresponding plurality of concentrates comprising a concentrate in substantially dry form, whereby in use the concentrate in the substantially dry form can be at least partially dissolved to be included in the peritoneal dialysis solution.

[0032] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for

the preparation of a dialysis solution comprising a plurality of compartments including a first compartment, a corresponding plurality of chemical components for forming the dialysis solution including a first chemical component disposed in the first compartment comprising glucose in substantially dry form, a mixing module, and a plurality of flow paths for fluid communication of a liquid between the mixing module and the plurality of compartments to provide a plurality of chemical component solutions, including a first flow path for fluid communication between the mixing module and the first compartment to provide a glucose solution, the mixing module including a mixing chamber for mixing the glucose solution and the plurality of chemical component solutions so as to produce the dialysis solution.

[0033] In accordance with the present invention, a method is also provided for peritoneal dialysis treatment with a dialysis solution produced at a predetermined patient location from a dialysis apparatus comprising a plurality of compartments including a first compartment and a corresponding plurality of components for the dialysis solution including a first component in substantially dry form, the method comprising combining a liquid and a first plurality of the plurality of components to provide a first plurality of component solutions, mixing the first plurality of component solutions to form the dialysis solution, flowing the dialysis solution into the peritoneal cavity of a patient, and draining the dialysis solution from the peritoneal cavity.

[0034] In accordance with another embodiment of the method of the present invention, the method includes providing an aqueous solution for medical use from a plurality of chambers including a first chamber and a corresponding plurality of concentrates disposed in the plurality of chambers including a first concentrate in substantially dry form in the first chamber, the method comprising priming the first concentrate with water to produce a first dissolved concentrate, flowing the first dissolved concentrate through a first flow regulator

to provide a metered volume of the first concentrate, measuring the concentration of the metered volume of the first concentrate, whereby a first amount of the first concentrate is provided, and delivering the first amount of the first concentrate to a mixing vessel until the first amount comprises a predetermined amount of the first concentrate.

[0035] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for an aqueous solution for medical use from a plurality of concentrates including a first concentrate in substantially dry form comprising a plurality of chambers, including a first chamber containing the first concentrate, priming means including a first conduit for supplying water to the first chamber to provide a first dissolved concentrate, a mixer for receiving the first dissolved concentrate, a flow regulator associated with the first dissolved concentrate for supplying the first dissolved concentrate to the mixer, measuring means for measuring the concentration of the first dissolved concentrate, and a first pump for pumping a metered volume of the first dissolved concentrate by means of the flow regulator to the mixer, whereby a predetermined amount of the first dissolved concentrate is delivered to the mixer.

[0036] In accordance with another embodiment of the method of the present invention, a method is provided for the preparation of dialysis solution from a plurality of compartments and a corresponding plurality of chemical components in the plurality of compartments, the method comprising adding liquid to the plurality of compartments to form a plurality of dialysis solution constituents, combining a first plurality of the plurality of dialysis solution constituents excluding a portion of at least one of the plurality of dialysis solution constituents to provide the dialysis solution for use in a dialysis treatment session, and discarding the portion of the at least one of the plurality of dialysis solution constituents.

[0037] In accordance with another embodiment of the method

of the present invention, a method is provided for the preparation of a dialysis solution at a patient treatment location from a plurality of compartments and a corresponding plurality of chemical components disposed in the plurality of compartments, the method comprising adding a liquid to the plurality of compartments to provide a plurality of chemical component solutions, flowing the plurality of chemical component solutions to a mixer, monitoring the flow of at least one of the chemical component solutions to the mixer, and controlling the flow of at least one of the chemical component solutions based on the monitoring thereof.

[0038] In accordance with another embodiment of the method of the present invention, a method is provided for the preparation of a dialysis solution at a patient treatment location comprising adding liquid to a plurality of chemical components including a first chemical component comprising glucose to form a plurality of chemical components solutions including a first chemical component solution comprising a glucose solution, mixing the plurality of chemical component solutions in a mixing module to form the dialysis solution, and connecting the mixing module into fluid communication with a patient dialysate line to permit the dialysis solution to flow from the mixing module to the patient dialysate line.

[0039] In accordance with another embodiment of the method of the present invention, a method is provided for the preparation of a dialysis solution at a patient treatment location from a plurality of dialysis components including a first plurality of the plurality of dialysis components in substantially dry form, comprising priming the first plurality of the dialysis components to form a first plurality of dialysis component solutions, mixing at least a portion of the first plurality of dialysis components solutions to form a concentrate solution, and diluting the concentrate solution with liquid to form the dialysis solution.

[0040] In accordance with another embodiment of the method of the present invention, a method is provided for performing

a dialysis treatment using a plurality of chemical components to form a dialysis solution, the method comprising adding liquid to the plurality of chemical components to form a plurality of chemical component solutions, mixing at least a portion of the chemical component solutions in a mixing module to form a concentrated solution, diluting the concentrated solution in the mixing vessel with a liquid so as to form the dialysis solution, and dispensing the dialysis solution from the mixing module to a patient dialysate line.

[0041] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for the selective formulation of a dialysis solution comprising a container including a plurality of compartments, a corresponding plurality of chemical components disposed in the plurality of compartments, whereby the plurality of chemical components can be combined with liquid to form a plurality of constituents of the dialysis solution, at least one module including a plurality of flow paths coupled to the plurality of compartments, whereby a source of liquid can be applied to the plurality of flow paths to provide the liquid to the plurality of compartments to form the plurality of constituents of the dialysis solution, a mixing chamber in fluid communication with the plurality of flow paths whereby the plurality of constituents can flow into the mixing chamber, at least one flow regulator for regulating the flow of the constituents from the plurality of compartments to the mixing chamber, and a controller for controlling the at least one flow regulator whereby the amounts of the constituents flowing to the mixing chamber can be adjusted.

[0042] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for the preparation of peritoneal dialysis fluid at a treatment location, the apparatus comprising a plurality of chambers, a corresponding plurality of concentrates in each of the plurality of chambers, each of the plurality of concentrates comprising a constituent of the peritoneal dialysis fluid, a

mixer for mixing the plurality of concentrates with a liquid to produce the peritoneal dialysis fluid, a controller for selectively controlling the mixer for producing one of a plurality of peritoneal dialysis fluids having different predetermined formulations, a sterilizer for sterilizing at least one of the liquid and the peritoneal dialysis fluid, and a patient connector in fluid communication with the peritoneal cavity of a patient for providing the peritoneal dialysis fluid to the patient, the controller including input data means for receiving the predetermined formulations whereby the mixer can be selectively controlled to produce the predetermined formulation of the peritoneal dialysis fluid.

[0043] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for the preparation of a peritoneal dialysis fluid at a treatment location comprising a plurality of chambers, a corresponding plurality of concentrates comprising constituents of the peritoneal dialysis fluid comprising a plurality of electrolytes, a mixer for mixing the plurality of concentrates with a liquid to produce the peritoneal dialysis fluid, a controller for selectively controlling the mixer to produce one of a plurality of predetermined peritoneal dialysis fluid formulations having a predetermined concentration of the electrolytes, a sterilizer for sterilizing at least one of the liquid and the peritoneal dialysis fluid, and a connector for fluid connection with a patient.

[0044] In accordance with another embodiment of the apparatus of the present invention, apparatus is provided for the preparation of peritoneal dialysis fluid at a treatment location comprising a water inlet for receiving a supply of water from a water supply, a water purifier in fluid communication with the water inlet for purifying water from the water inlet, a mixer for mixing the purified water with dialysis fluid concentrate to produce a peritoneal dialysis fluid, a sterilizer in fluid communication with the mixer for sterilizing the peritoneal dialysis fluid, the sterilizer

comprising a heat sterilizer for heat sterilizing the peritoneal dialysis fluid at a sterilizing temperature and elevated pressure, and a connector in fluid communication with the sterilizer for providing fluid communication for the sterilized peritoneal dialysis fluid with the peritoneal cavity of a patient.

[0045] In accordance with another embodiment of the method of the present invention, a method is provided for dialysis treatment of a patient with a dialysis treatment system including a connector and flow path, the method comprising connecting a patient dialysate conduit with the connector, flowing a dialysis solution along the flow path to the patient dialysate conduit, sterilizing the dialysis solution flowing to the patient dialysis conduit at a sterilization module in the dialysis treatment system, and sterilizing at least a substantial portion of the flow path including flowing a sterilization liquid in the flow path between the sterilization module and the connector.

[0046] In accordance with the present invention, a dialysis system is also provided for providing a dialysis solution from tap water at a patient treatment location comprising a water treatment module for purifying the tap water, a mixing module connected to the water treatment module for mixing the purified tap water with a plurality of chemical components to provide the dialysis solution, and a connector connected to the mixing module and adapted to be connected to a patient dialysate conduit for flowing the dialysate solution thereto.

[0047] In accordance with another embodiment of the apparatus of the present invention, an apparatus is provided for providing a predetermined dialysis solution from a plurality of dialysis components utilizing predetermined prescription information comprising a processor for processing the predetermined prescription information, a mixing module for mixing the plurality of dialysis components to form the dialysis solution, a controller for controlling the mixing module based on the predetermined prescription information

whereby the mixing module can form the dialysis solution with predetermined required amounts of each of the plurality of dialysis components.

[0048] In accordance with another embodiment of the method of the present invention, a method has been provided for peritoneal dialysis using a dialysis solution prepared at a patient treatment location based on predetermined prescription information, the method comprising providing a processor disposed at the patient treatment location for forming the dialysis solution from a plurality of dialysis components, providing the processor with a container including a predetermined quantity of each of the plurality of dialysis components whereby a plurality of different formulations of the dialysis solutions can be prepared therefrom, processing information regarding the predetermined prescription information in the processor, forming a predetermined formulation of the dialysis solution in the processor based on the predetermined prescription information, connecting the processor to the peritoneal cavity of the patient, flowing the predetermined formulation of the dialysis solution into the peritoneal cavity, removing the predetermined formulation of the dialysis solution from the peritoneal cavity, and disengaging the container from the processor.

[0049] In accordance with the present invention, dialysis apparatus is also provided comprising a water purification module including an inlet for tap water, at least one particulate filter in fluid communication with the inlet, a degasser for removing gas from the tap water, a first reverse osmosis membrane unit including a first inlet, a first purified water outlet, and a first waste water outlet, a second reverse osmosis membrane unit including a second inlet, a second purified water outlet, and a second waste water outlet, the first purified water outlet being in fluid communication with the second inlet and the second waste water outlet being in fluid communication with the first inlet, a thermal control and sterilization module in fluid

communication with the water purification module and including a plurality of heat exchangers for conducting heat transfer between fluids flowing therein, a concentrate mixing module in fluid communication with the water purification module and the thermal control and sterilization module, the concentrate mixing module comprising a plurality of compartments, a corresponding plurality of concentrated components of the dialysis solution within the plurality of compartments, a plurality of fluid couplers including fluid channels including a first plurality of the fluid couplers adapted to be in fluid communication with predetermined one of the plurality of compartments, a plurality of valves for liquid flow regulation including a first plurality of the valves associated with a corresponding plurality of the plurality of fluid couplers whereby the flow of liquid to and from the plurality of compartments can be regulated thereby, a concentrate reservoir in fluid communication with the plurality of fluid couplers, at least one conductivity sensor for sensing the conductivity of a liquid flowing into the concentrate reservoir, a mixing chamber in fluid communication with the concentrate reservoir and with one of the first and second purified water outlets for forming the dialysis solution, at least one pump in fluid communication with the plurality of flow couplers, the concentrate reservoir and the mixing chamber, an outflow drain for discarding the liquid, and a connector for fluid communication with a patient dialysate line, the connector in fluid communication with the mixing chamber whereby the dialysis solution can flow to the patient dialysate line.

[0050] Accordingly, the present invention is directed to apparatus and methodology that substantially obviate one or more of the short-comings or disadvantages of the relevant art.

[0051] One object of the present invention is to prepare a medical fluid at a patient treatment site by mixing substantially water with one or more concentrates. The fluid may be prepared with ordinary tap water. As a result, a

patient's treatment requirements can be met through a compact package of concentrates, as opposed to multiple bags of fluid. This is convenient both for the patient and for the patient's doctor. It also reduces weight and volume and, accordingly, storage and transportation costs, as well as improving the logistics. Fewer disposable components may be used, involving the use of less plastic, and giving significant environmental advantages.

[0052] Another object of the present invention is to provide one or more components of medical fluid in at least substantially dry form to increase shelf life and/or problems associated with component precipitation. At least glucose may be provided in substantially dry form.

[0053] An additional object of the present invention is to provide a universal or near-universal (referred to as "universal" herein) container for filling multiple patient prescriptions. The administering machine is controlled to mix the appropriate prescription at the treatment site. As a result, multiple prescriptions can be obtained using a universal container or cartridge. This reduces the need to inventory multiple prescriptions.

[0054] Still another object of the present invention is to provide a container containing at least one concentrate in combination with a cleaning agent. In this way, the treatment and cleaning agents are conveniently packaged together.

[0055] Yet another object of the present invention is to provide a medical treatment apparatus having a reduced number of aseptic connections. There may be zero or only one aseptic connection. This reduces the risk of infections such as peritonitis.

[0056] A further object of the present invention is to provide a system whereby a patient's prescription can be electronically communicated to the dialysis machine, such as through a smart card. In this way, if a patient's prescription changes, the machine can be reprogrammed, while continuing to use the same universal cartridge.

[0057] A yet further object of the present invention is to provide a system offering higher fluid doses in peritoneal dialysis treatment without significant additional cost, unlike in conventional peritoneal dialysis systems in which the cost is roughly proportional to the fluid volume. Higher fluid volumes also may mean that a patient, who would normally be switched from conventional PD to another mode of treatment, such as hemodialysis (HD) because conventional PD provides inadequate treatment, may be kept on PD for a longer time.

[0058] A still further object of the present invention is to provide a system for sterilizing peritoneal dialysis fluid immediately before delivery to a patient in order to minimise the chance of viable bacteria entering the peritoneum.

[0059] It should be understood that the present invention could still be practised without performing one or more of the objects and/or advantages set forth above, or by imperfectly performing certain of the objects and/or advantages. Still other objects and advantages will become apparent from the following description of the invention and the claims.

[0060] To achieve these and other objects and advantages, and in accordance with the purpose of the present invention, as embodied and broadly described herein, the invention includes a number of embodiments.

[0061] Viewed from a first aspect, the present invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:
a plurality of chambers, each containing a respective concentrate of a constituent of the peritoneal dialysis fluid;
a fluid mixer arranged to mix the concentrates with liquid to produce peritoneal dialysis fluid;
a sterilizer arranged to sterilize at least one of the liquid and the peritoneal dialysis fluid; and
a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal cavity of a patient, and furthermore wherein

at least one of the concentrates is in substantially dry form and, in use of the apparatus, it is at least partially dissolved to form part of the peritoneal dialysis fluid.

[0062] The present invention also provides a method of producing peritoneal dialysis fluid at a treatment location and introducing the fluid into the peritoneal cavity of a patient, the method comprising:

providing a plurality of concentrates of constituents of the peritoneal dialysis fluid in respective chambers;

mixing the concentrates with liquid to obtain peritoneal dialysis fluid;

sterilizing at least one of the liquid and the peritoneal dialysis fluid; and

introducing the peritoneal dialysis fluid to the peritoneal cavity of a patient; and furthermore wherein

at least one of the concentrates is in substantially dry form and is at least partially dissolved to form part of the peritoneal dialysis fluid.

[0063] By providing a concentrate in substantially dry or solid form, for example as a powder, the problems associated with liquid concentrates, such as precipitation, short shelf-life etc., can be minimised.

[0064] At least one of the concentrates is an osmotic agent, such as a carbohydrate, gluconate, peptides, ketoacid, glycerol, glucose polymer, disaccharide, etc. In one embodiment, the osmotic agent is glucose or dextrose. When glucose is provided as a solution, it generally has a limited shelf-life before it has to be used. By providing the osmotic agent in substantially dry or solid form and then dissolving it at the point of use, its shelf-life may be increased.

[0065] At least one of the concentrates is a buffer, such as bicarbonate, lactate, acetate, pyruvate, hydroxybutyrate, phosphate, etc. In one embodiment, sodium bicarbonate or sodium lactate or a combination thereof is used as a buffer. By providing sodium bicarbonate in substantially dry or solid form, problems with solutions degrading by the precipitation

of solids can be avoided. Sodium bicarbonate is sometimes favored as a buffer for physiological reasons, but often another buffer is used in peritoneal dialysis. Thus, the use of substantially dry sodium bicarbonate, which is then freshly dissolved into solution at a treatment location, in a peritoneal dialysis treatment system, is beneficial.

[0066] A concentrate provided in a particular chamber may comprise more than one substance, for example some or all of the electrolytes may be provided in one chamber, and an osmotic agent may be provided in another chamber. In one embodiment, each concentrate comprises a separate constituent substance of the peritoneal dialysis fluid. For the production of a peritoneal dialysis fluid, each chamber may contain a separate constituent substance of the peritoneal dialysis fluid, selected from a group comprising: sodium chloride, sodium bicarbonate, magnesium chloride, calcium chloride, sodium lactate, lactic acid and glucose.

[0067] One or more of the concentrates may be provided in liquid form, and one or more of the concentrates may be provided in substantially dry form. In one embodiment the concentrates comprise: sodium chloride in substantially dry form; sodium bicarbonate in substantially dry form; magnesium chloride in substantially dry form; calcium chloride in substantially dry form; lactic acid solution; and glucose in substantially dry form.

[0068] By providing a plurality of concentrates of the constituents of peritoneal dialysis fluid in respective chambers, in accordance with the first aspect of the present invention, it becomes possible to produce peritoneal dialysis fluids of different formulations. The apparatus comprises a controller for controlling the fluid mixer to produce such different formulations. There is thus provided a choice of formulations which can be made using the plurality of concentrates and liquid, such as purified water. For example, a single disposable container containing the concentrates can be used to produce different formulations as required by a

prescription of a patient. This is considerably more convenient than the currently available systems for providing peritoneal dialysis fluids to a patient, in which the manufacturer stocks a range of bags of fluids of different formulations and the user has to be supplied with and choose the right bag for his or her treatment. Instead, the user can always be supplied with the same plurality of concentrates, which can then be used by the apparatus to make the required formulation.

[0069] In one embodiment, the concentrates comprise a plurality of electrolytes and the controller is operable to produce peritoneal dialysis fluid formulations having different relative concentrations of electrolytes. Thus, rather than being able merely to vary the concentration of osmotic agent (e.g. glucose), the apparatus can vary the relative concentrations of the electrolytes in the peritoneal dialysis fluid according to a patient's prescription. This is an advance over the previously proposed systems for producing peritoneal dialysis fluid at a treatment location using a single combined source of electrolytes. The electrolytes used in the peritoneal dialysis fluid may be one or more of sodium bicarbonate, sodium chloride, sodium lactate, magnesium chloride and calcium chloride.

[0070] The controller is in one embodiment provided with data input means for receiving prescription information for a patient. Such data input means may comprise a keyboard or touch screen or the like for a person to input the required prescription information. In one embodiment, the data input means comprises a memory device, for example a smart card, which may be inserted in a suitable part of the apparatus. Alternatively, or additionally, the data input means may comprise a modem or other means enabling remote communication, for example for supervision or for transmission of prescription information to the apparatus.

[0071] It is possible to effect dissolution of substantially dry or solid concentrates in the chamber in

which it is supplied. In the case of some concentrates, a relatively large quantity of solution may be needed, such that the chamber will generally not be large enough, without becoming cumbersome, to receive enough water to dissolve all the concentrate. Examples of such concentrates in a peritoneal dialysis solution are sodium chloride and sodium bicarbonate. In these cases, more than a single chamber volume of water is used to dissolve the concentrate. One way of doing this would be to fill the chamber with water through an opening, to then empty the chamber by reversed flow through the same opening, using an air vent to allow air to fill the chamber during emptying (if the chamber walls are relatively rigid, an air vent not being necessary in the case of a flexible walled chamber). Filling would then take place again, and the process would be repeated as many times as necessary.

[0072] In another embodiment, the apparatus is arranged to prime the at least one concentrate in substantially dry form in a respective chamber with liquid comprising water, the amount of concentrate in the chamber and the size of the chamber being such that the concentrate is only partially dissolved when the chamber is filled with liquid, the apparatus further comprising a flow line for removing liquid comprising dissolved concentrate from the chamber, and a flow line for substantially simultaneously adding the same amount of liquid as removed to the chamber.

[0073] With such an arrangement, after initial priming a continuous flow to the fluid mixer can be obtained, rather than a periodic flow, reducing the number of cycles required, and thus the opportunities for inaccuracies, for a given batch of peritoneal dialysis fluid. Thus, two flow lines are provided for simultaneous use. One of these may conveniently be used for priming, and the other for venting air from the container, an air vent being necessary in the case of a rigid walled chamber. The concentrate removal flow line may be used during priming to introduce the liquid comprising water to the chamber, and the liquid adding flow line is used during

priming to vent air from the chamber. During normal use, venting is not required.

[0074] Such a first type of chamber or partial dissolution chamber is suitable for containing sodium chloride or sodium bicarbonate for making the peritoneal dialysis fluid.

[0075] A second type of chamber is contemplated for other constituents of the peritoneal dialysis fluid, such as calcium chloride and magnesium chloride. In the case of these concentrates, they are generally only required in relatively small quantities and at low concentrations in the peritoneal dialysis fluid, and so a relatively small chamber can have an adequate volume such that one liquid fill will result in a sufficient amount of dissolved concentrate. Therefore, the apparatus may be arranged to prime the at least one concentrate in substantially dry form in a respective chamber with liquid comprising water, the amount of concentrate in the chamber and the size of the chamber being such that the concentrate is fully dissolved when the chamber is filled with liquid. With this type of chamber, the priming inflow can conveniently use the same flow line as that used to remove dissolved concentrate from the chamber. In the case of a rigid walled chamber, an air vent may be provided to vent air during priming and emptying.

[0076] A third type of chamber may be used for the osmotic agent, normally glucose. It is provided in substantially dry or solid e.g. powder form, and the apparatus will then be suitably equipped to stir, agitate or recirculate the glucose once liquid comprising water has been added. This is because of the relative difficulty in achieving rapid dissolution of glucose. In one embodiment of the apparatus, a respective chamber contains an osmotic agent, e.g. glucose, and the apparatus comprises a flow circuit for introducing liquid comprising water into the osmotic agent chamber, for removing liquid comprising dissolved osmotic agent from the chamber and for re-introducing the liquid comprising dissolved osmotic agent into the chamber. Dissolution, e.g. of glucose, is

generally promoted by heating the diluent liquid, for example to 40°C. Heated liquid may initially be supplied to the glucose chamber. It is desirable to maintain the glucose heated during dissolution and circulation, and advantageously therefore a heater is provided for heating the liquid comprising dissolved glucose as it circulates round the flow circuit.

[0077] Since glucose powder tends to release gas bubbles during dissolution, the apparatus may have a vent to allow escape of gas as the liquid comprising dissolved glucose circulates around the flow circuit.

[0078] The plurality of chambers containing respective concentrates may be provided by more than one container. It is, however, convenient for a user if all the ingredients for making the peritoneal dialysis fluid are provided in a single container. In one embodiment, the plurality of chambers are defined by a disposable container. In another embodiment, each chamber is in the form of a compartment of a container.

[0079] It will thus be appreciated that a plurality of different types of chambers may be provided to deal with the different requirements of the different constituents of the peritoneal dialysis fluid, i.e. taking account of the amount of each constituent normally required and the ease or difficulty in dissolving each constituent. From the user's perspective, however, there is the benefit that all the chambers and the constituents of the peritoneal dialysis fluid which they contain can be provided in a single container. This can provide all constituents needed for an overnight peritoneal dialysis treatment session, which may for example involve the use of from about 8 to 30 liters of peritoneal dialysis fluid or more, without the user having to set up the several bags of fluid which would be required with conventional peritoneal dialysis treatment.

[0080] It is possible to support the container on the apparatus in a fixed position and then for the apparatus to have a chamber communicating portion, e.g. a spike, which

moves to a position communicating with the interior of the chamber. In one embodiment, the apparatus comprises a container engaging portion for engaging the container and urging the container to a position in which the chambers are opened for communication with respective portions of the apparatus.

[0081] In general, it will be desirable to place the container in a location where it can be engaged by the container engaging portion. One way of doing this is for a user to slide the container to the engagement location in a first direction, for example in a horizontal direction, and then for the container engaging portion to urge the container to the communicating position in a second direction, for example in a vertical direction.

[0082] The container engaging portion may, for example, engage a region of the container remote from the region of the chambers where they are to be opened. This may be the base of the container, inverted so that its opening region faces downwardly. In one embodiment, the container engaging portion is arranged to engage a plurality of flanges each provided adjacent to a respective opening of a respective chamber. By effecting engagement adjacent to the openings, reliable urging in the opening region of the container may be achieved. The flanges are, for example, formed on the necks defining the openings of the respective chambers.

[0083] In one embodiment, a flange associated with each opening is engaged, to ensure reliably and positively that each opening is communicated with the chamber communicating portions of the apparatus. It will be appreciated that it is important that all intended communicating paths should be created at the interface between the apparatus and the container. In one exemplary container, there are eight chamber openings where communication is to be effected. One embodiment of the arrangement for achieving the desired reliable interface involves that at least two of the container openings being linearly aligned with each other, and the container

engaging portion comprising a pair of laterally spaced members arranged to engage flanges defined on opposite sides of the openings.

[0084] In one embodiment of the apparatus, a plurality of spikes are provided for penetrating respective seals of the chambers to open the chambers. Each spike advantageously comprises two fluid flow channels, to allow simultaneous inflow and outflow of liquid or gas to or from the chamber. As will be apparent from the description below, in the case of a chamber containing glucose it is useful to provide three flow channels, whereas for other concentrates two channels are provided. Rather than having to provide a three flow channel spike, there is provided a pair of spikes for penetrating an osmotic agent, e.g. glucose, containing chamber. This can provide three flow channels, two contributed by one spike and the third by the other spike. In addition, since the osmotic agent chamber will usually be substantially larger than the other chambers, there will be sufficient space on the osmotic agent chamber wall for the provision of two openings.

[0085] After the container has been used to supply the ingredients for one or more peritoneal dialysis patient fills, it will be removed and on the next treatment occasion a fresh container will be used. It is beneficial to disinfect the spikes between treatments. The apparatus comprises a cover for covering the spike when the container is removed to enable the spike to be disinfected. The container engaging portion may be arranged to engage the cover to urge it to its covering position. Thus, the container engaging portion can fulfil both the function of urging the container to its communicating position, and that of urging the cover to its covering position when no container is present.

[0086] It will be appreciated that the container described herein embodies a number of inventive aspects. A second aspect of the present invention is therefore concerned with a container, such as a disposable container.

[0087] In one form of the second aspect, the present

invention provides a container containing, in concentrated form, all of the concentrates, which, when mixed with water, provide sufficient peritoneal dialysis fluid for a full peritoneal dialysis treatment session.

[0088] In another form of the second aspect, the present invention provides a container containing concentrated components of dialysis fluid, the container comprising a chamber containing powdered glucose and at least one other distinct chamber containing at least one powdered inorganic salt.

[0089] In another form of the second aspect, the present invention provides a container containing concentrated components of dialysis fluid, the container comprising at least one chamber containing a cleaning agent and at least one other distinct chamber containing at least one powdered inorganic salt. It is advantageous to provide a cleaning agent in the same container as at least one concentrate for making peritoneal dialysis fluid, as this facilitates operation of the apparatus, because the user is only required to insert one container into the apparatus to provide the concentrated PD fluid and to provide the cleaning agent, rather than separate containers which may be mistaken.

[0090] In another form of the second aspect, the present invention provides a container containing concentrated components of dialysis fluid, the container having defined therein at least two distinct chambers, each of the chambers containing a different inorganic salt, wherein the volume of each of the chambers and the amount of salt contained within each chamber is such that when a solution of each salt is prepared by filling each of the chambers with liquid, such as water, the conductivities of the solutions so prepared are characteristically different. As described in more detail below, such an arrangement enables the apparatus with which the container is to be used to check that it is receiving the correct concentrate or inorganic salt from each chamber.

[0091] In another form of the second aspect, the present

invention provides a container containing concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising at least one connector associated with each chamber, wherein each the connector comprises at least two separate fluid channels, permitting simultaneous inflow to and outflow from the respective chamber. This arrangement allows gas to exit the chamber through one fluid channel as liquid enters through the other fluid channel, and/or it allows gas to enter the chamber through one fluid channel as liquid exits via the other fluid channel, and/or it allows replacement liquid to enter the chamber as liquid exits the chamber. Such an arrangement is particularly useful in the case of chambers having relatively rigid rather than flexible (i.e. collapsible) walls, where the volume of the chamber remains substantially constant whether it is empty or full. By providing the at least two fluid channels as part of the connector, as distinct from providing a vent elsewhere on the chamber, the two fluid channels can be opened up and established only at the time when the container is to be used, such as simultaneously, for example by breaking a seal which may be in the form of a membrane or septum.

[0092] In one arrangement, the at least two fluid channels are arranged concentrically in each of the connectors. This type of connector can, for example, conveniently mate with a spike which itself has two fluid channels, as described above.

[0093] In the case of an osmotic agent, e.g. glucose, containing chamber, it is useful to have more than two fluid channels, notably three. In one embodiment, at least one of the chambers comprises two connectors, one such connector comprising the at least two separate flow channels, and the other connector comprising a further fluid channel.

[0094] Again in the case of an osmotic agent, e.g. glucose, dissolution thereof can be advantageously promoted by providing one of the fluid channels with a diffuser to diffuse an inflow of liquid into the chamber.

[0095] In one embodiment, the connectors are provided, during operation, in a lower region of the chambers, and one of the fluid channels of at least one connector has a portion extending to an upper region of the chamber. The portion in the upper region can, for example, be used as an air vent, as an inlet for replacement liquid, or for recirculation.

[0096] As explained above, at least some of the openings to the chambers are in alignment with each other. Their openings are mutually aligned along the linear axis. Thus, the connectors can all be engaged by a container engaging portion of the apparatus. The connectors may comprise neck portions each formed with an external flange for engagement by the container engaging portion. A pair of flanges may be provided on opposite sides of the neck portion, or a single flange may extend circumferentially round the neck portion. The container engaging portion may then be in the form of a pair of laterally spaced members - a fork - for engagement with the flanges.

[0097] The container should be mountable on or insertable into the machine in a unique manner, to ensure that the correct connectors align with the required communicating portions of the apparatus. In one embodiment, the linear axis of the mutually aligned connectors is offset from a central axis of the container. The container can then interface with the apparatus in the correct manner only.

[0098] In another form of the second aspect of the present invention, there is provided a container for use in priming powdered glucose at a patient treatment location, comprising an inlet port in a lower region of the container for receiving a supply of water to dissolve the powdered glucose in the container, wherein the inlet port is provided with a diffuser which is arranged to diffuse the flow of water into the powdered glucose.

[0099] In another form of the second aspect of the present invention, there is provided a container for concentrated components of dialysis fluid, the container having defined

therein a plurality of distinct chambers, the container comprising at least one connector associated with each chamber, wherein at least two of the connectors are mutually aligned along a linear axis.

[0100] In another form of the second aspect of the present invention, there is provided a container for concentrated components of dialysis fluid, the container having defined therein a plurality of distinct chambers, the container comprising a container body and at least one connector associated with each chamber, wherein there is at least one axis about which the container body is substantially rotationally symmetric, and wherein the connectors are arranged relative to the container body such that the arrangement of connectors is rotationally asymmetric about the axis.

[0101] In the manufacture of the container, each chamber may be charged with the appropriate concentrate. It may be problematic to successively charge each chamber of a single container. Therefore, the container may be made as a plurality of sub-containers which are later connected together.

[0102] In another form of the second aspect of the present invention, the invention provides a method of manufacturing a container for concentrated components of dialysis fluid, the method comprising the steps of:
manufacturing a plurality of individual sub-containers; and
connecting the sub-containers to form the container.

[0103] The present invention also extends to a container made by the above method.

[0104] The apparatus may be connected to a source of purified water, for example a reverse-osmosis unit. In one embodiment, the apparatus comprises a water purifier. The water purifier may, for example, comprise one or more reverse osmosis membrane units. In one embodiment, the water purifier comprises a first reverse osmosis membrane unit, and a second reverse osmosis membrane unit. Each membrane unit has an inlet, a purified water outlet and a waste water outlet. In

one embodiment, the purified water outlet of the first membrane unit is in fluid communication with the inlet of the second membrane unit. Moreover, the waste water outlet of the second membrane unit may be in fluid communication with the inlet of the first membrane unit.

[0105] According to this arrangement, the water from the waste water outlet of the second RO membrane unit, which is already reasonably pure because it has been through the first RO membrane unit, is recycled and passes through the first RO membrane unit again, so that the overall water consumption of the apparatus is reduced. In this way, two RO membrane units can be used, in order to provide a higher purity of water, without increasing the overall water consumption of the apparatus.

[0106] The water purifier may comprise, for example upstream of the inlet of the RO membrane unit, a coarse filter (for example a 30 micron filter), a fine filter (for example a 5 micron filter), a charcoal filter and/or a water softener. Each of these components prevents blocking of the reverse osmosis membranes.

[0107] The water purifier may further comprise a degassing arrangement upstream of the first (or second) RO membrane unit. The water is degassed before it passes through the RO membranes, as a reduction in the amount of dissolved carbon dioxide and other gases in the water can improve the performance of the RO membrane(s). Furthermore, gas bubbles in the water can interfere with the correct operation of the pumps and the like. In general, it is desirable for the water to be degassed at an early stage in the production of the peritoneal dialysis fluid, as this simplifies the further processing steps, because the dissolved gas content of the water is fixed.

[0108] In one embodiment, the sterilizer is a heat sterilizer.

[0109] Viewed from a third aspect, the present invention provides apparatus for the production of peritoneal dialysis

fluid at a treatment location comprising:

a water inlet for receiving a supply of water from a mains water supply;

a water purifier for purifying the supply of water from the water inlet;

a fluid mixer for mixing dialysis fluid concentrate with the purified water supply to produce a supply of peritoneal dialysis fluid;

a sterilizer for sterilizing the supply of peritoneal dialysis fluid; and

a fluid outlet arranged to communicate the sterilized supply of peritoneal dialysis fluid to the peritoneal cavity of a patient; and further wherein

the sterilizer is a heat sterilizer arranged for heat sterilization of the peritoneal dialysis fluid at a sterilizing temperature and at an elevated pressure.

[0110] Heat sterilization is generally considered to be effective and safer than, for example, bacterial filtering.

[0111] In one embodiment, the sterilizer is provided downstream of the fluid mixer so that any bacteria introduced into the peritoneal dialysis fluid during mixing are neutralised. In this way, the production costs of the container for the concentrated components can be reduced, because the components need not be pre-sterilized.

[0112] Although the sterilizer may be configured to sterilize the peritoneal dialysis fluid itself, alternatively one or more sterilizers may be provided for sterilizing one or more of the components of the peritoneal dialysis fluid, such as the liquid, for example water, used to form the peritoneal dialysis fluid and/or the concentrated solutions. If the concentrates are provided as sterile concentrates, only the water used to form the peritoneal dialysis fluid is sterilized.

[0113] The sterilizer may comprise a sterilization flow passage and is arranged to heat sterilize the peritoneal dialysis fluid as it flows along the sterilization flow

passage, so that the flow of peritoneal dialysis fluid does not need to be stopped for heat sterilization. In one embodiment, the apparatus comprises a flow path downstream of the heat sterilizer for the flow of sterilized peritoneal dialysis fluid to the patient fill connection, and cooling means for cooling the sterilized peritoneal dialysis fluid as it flows along the flow path, in order that the peritoneal dialysis fluid may be brought to body temperature when it reaches the patient fill connection. The apparatus may be arranged to heat sterilize the flow path prior to its use for the flow of sterilized peritoneal dialysis fluid to the patient fill connection, to ensure that the sterilized fluid travels along a sterilized path.

[0114] A fourth aspect of the present invention is concerned with systems for dissolving a substantially dry concentrate and delivering the dissolved concentrate to a mixing vessel.

[0115] Viewed from a fourth aspect therefore the present invention provides apparatus for the production of an aqueous solution for medical use from a plurality of concentrates, the apparatus being arranged to communicate with a plurality of chambers each containing a respective concentrate, at least one of the concentrates being in substantially dry form, the apparatus comprising:

at least one flow line arranged to prime the at least one concentrate in substantially dry form with liquid comprising water to form at least one dissolved concentrate;

a mixing vessel arranged to receive the at least one dissolved concentrate;

a flow regulator associated with the at least one dissolved concentrate arranged to pass the concentrate to the mixing vessel; and further comprising

measuring means arranged to measure a concentration of the at least one dissolved concentrate; and

a pump arranged to pump a metered volume of the at least one dissolved concentrate by means of the associated flow

regulator to the mixing vessel, while measuring by the measuring means the concentration of the dissolved concentrate, so as to deliver a predetermined amount of the dissolved concentrate to the mixing vessel.

[0116] The present invention also provides a method of providing an aqueous solution for medical use from a plurality of concentrates, comprising:

providing a plurality of concentrates in separate chambers, at least one of the concentrates being in substantially dry form; priming the at least one concentrate in substantially dry form with liquid comprising water to form at least one dissolved concentrate;

passing the at least one dissolved concentrate to a mixing vessel by means of a flow regulator associated with that concentrate; and further including

adjusting the flow regulator associated with the at least one dissolved concentrate for passing a metered volume of the concentrate through the flow regulator;

measuring a concentration of the concentrate to determine an amount of the concentrate delivered to the mixing vessel; and terminating the delivering of concentrate when a predetermined amount has been delivered.

[0117] Thus, from a starting point of concentrates at least one of which is in substantially dry form, e.g. powder, an aqueous solution may be obtained in a mixing vessel comprising a predetermined amount of each concentrate, and hence having each concentrate present in a predetermined concentration ratio. Such solution can be prepared to a precise desired formulation, and may be put to medical use, for example for the purposes of peritoneal dialysis, hemodialysis, hemofiltration or hemodiafiltration.

[0118] In general, it is intended to obtain a flow of concentrate at a predetermined concentration and this may take time to develop, for example because time is required to achieve dissolution or because adjustments are made e.g. dilution to achieve a flow at the predetermined concentration.

It is beneficial to use the flow as soon as it is established at the desired concentration, rather than to send it to drain while awaiting a similar establishment for another concentrate. By providing a mixing vessel in which a known amount of concentrate is to be stored, that concentrate can be passed to the mixing vessel without delay and thus without significant loss to drain.

[0119] Where a plurality of concentrates are provided in substantially dry form, each such concentrate is primed to form a dissolved concentrate, a metered volume of each dissolved concentrate is pumped by means of its associated valve to the mixing vessel, while measuring the concentration of the dissolved concentrate, so as to deliver a predetermined amount of the dissolved concentrate to the mixing vessel. Thus, an aqueous solution is obtained comprising a predetermined amount of each concentrate.

[0120] Where one or more concentrates are initially provided in liquid form, they may be provided at a known concentration, in which case the concentration measuring step may not be necessary, it being sufficient to pump a metered volume to the mixing vessel. However, to be sure of obtaining the right amount of all concentrates in the mixing vessel, it is possible to measure the concentration of such initially liquid concentrates as they are passed to the mixing vessel. This would also be useful where a concentrate is provided initially in liquid form at a concentration which is only approximate. An example of a concentrate which may be provided in liquid form to make *e.g.* peritoneal dialysis fluid is lactic acid.

[0121] Another method therefore comprises adjusting a first flow regulator associated with a first concentrate for passing the first concentrate through the first flow regulator at a metered rate, measuring a concentration of the first concentrate to determine an amount of the concentrate delivered to the mixing vessel, terminating the delivering of the first concentrate when a predetermined amount has been

delivered, adjusting a second flow regulator associated with a second concentrate for passing the second concentrate through the second flow regulator at a metered rate, measuring a concentration of the second concentrate to determine an amount of the concentrate delivered to the mixing vessel, terminating the delivering of the second concentrate when a predetermined amount has been delivered, and repeating the adjusting, passing, measuring and terminating for each further concentrate, thereby to provide an aqueous solution comprising a predetermined amount of each concentrate. Such a method is applicable to a plurality of concentrates in which at least one is provided in substantially dry form, i.e. there may initially be a plurality, one or no concentrates provided in liquid form. To make dialysis fluid, for example, the electrolytes and osmotic agent may be provided as solid concentrates, e.g. powders, while an acid may be provided as a liquid concentrate.

[0122] In one embodiment, the apparatus comprises a flow regulator associated with each concentrate, wherein in use of the apparatus a metered volume of each concentrate is pumped by means of its associated valve to the mixing vessel, while measuring the concentration of the concentrate, so as to deliver a predetermined amount of the concentrate to the mixing vessel. For example, there may be a first flow regulator associated with a first concentrate, a second flow regulator associated with a second concentrate, and a further flow regulator associated with each further concentrate.

[0123] The pumping of concentrate flows may be effected by a plurality of devices, such as metering pumps, for example one associated with each concentrate. In one embodiment, the pump is arranged for pumping, in turn, each concentrate to the mixing vessel. Thus, the use of a pump associated with each concentrate can be avoided, thereby reducing the cost, size and weight of the system, particularly where several concentrates are involved, as will be the case for dialysis liquids, for example.

[0124] Similarly, although a plurality of concentration measuring means may be provided, again one associated with each concentrate, each concentrate may alternatively be passed through the same measuring means. This may reduce the cost, size and weight of the system. In addition, because the measuring means measures the concentration of each concentrate individually, it can be selected or set up to give accurate measurements over a range wide enough to cover the expected individual concentrations. This is intended in a system in which a measuring means is used to measure e.g. the conductivity of the solution accumulating in the mixing vessel, since the conductivity will increase as additional concentrates are added and the measuring means would then be required to be accurate over a wide range, i.e. a range sufficient to cover the conductivity of a first concentrate, the higher conductivity of a first and second concentrate combined, etc. Furthermore, in such a cumulative system, measurement errors resulting from the measurement of the first concentrate will add to the errors in the measurement of the second concentrate and so on, so that later concentrates are measured at a lower accuracy than initial ones. This does not occur when the concentration of each concentrate is measured individually as the errors are due only to the measurement being taken.

[0125] The measuring means may comprise more than one measuring device, such as two measuring devices, to provide the system with redundancy and thus additional safety. The measuring means may comprise a pH meter or other type of meter, such as an ion selective meter, but preferably comprises a conductivity meter.

[0126] The apparatus may be arranged to dilute a concentrate after it leaves its respective chamber and before it is passed to the mixing vessel. By controlling the amount of dilution, the concentration of the constituent substance delivered to the mixing vessel can be controlled to a predetermined concentration, even starting from different pre-

dilution concentrations, which may often be the situation in the case of a concentrate initially provided in substantially dry form. The dilution may for example be effected by a proportioning pump. In one dilution arrangement, it comprises a concentrate flow line along which concentrate is pumped by the pump at a metered rate, a water flow line along which water is pumped by a second pump at a metered rate, the concentrate flow line joining the water flow line so that in use the concentrate and water are mixed to dilute the concentrate before it is passed to the mixing vessel. The concentration of the concentrate or diluted concentrate is measured, and the pumps are controlled to provide a dilution ratio required in order to obtain a desired concentration of the diluted concentrate.

[0127] A convenient method of achieving the delivery of a predetermined amount of concentrate to the mixing vessel comprises passing the diluted concentrate to the mixing vessel at a flow rate, measuring the concentration of the diluted concentrate, multiplying the measured concentration with the flow rate, integrating the product of the multiplication over time to obtain a total amount of concentrate material delivered to the mixing vessel, and terminating the passing of diluted concentrate to the mixing vessel when a predetermined amount of concentrate material has been delivered to the mixing vessel. The apparatus may therefore include a suitable processor for carrying out the multiplying, integrating and terminating functions.

[0128] The plurality of chambers containing concentrates will normally be provided in predetermined positions relative to each other and relative to the apparatus to ensure that each concentrate is supplied to the appropriate portion of the apparatus. In one embodiment, the apparatus is able to check that it has received the correct concentrate at each appropriate portion. Therefore, the method comprises measuring a property of a concentrate or a property of the concentrate after dilution thereof downstream of its respective chamber,

and determining from that measurement if the concentrate is the concentrate expected from that chamber.

[0129] While the measured property may be pH, for example, it may be difficult to distinguish between concentrates which have a neutral pH at any concentration. In one embodiment, the measured property is conductivity. The concentrates may be provided in amounts in their respective chambers such that when their properties e.g. conductivities are later measured they are distinguishable from each other. The property may be measured in its form as supplied from the chamber, i.e. without further dilution. If it is measured after dilution, then providing dilution is effected by the addition of a known amount of liquid comprising water, then the measurement for the expected concentrate can still be known.

[0130] The concentration of the concentrates in the mixing vessel may provide the final formulation for the required medical use. However, in order that the mixing vessel can be kept to a reasonable size, in one embodiment, the liquid in the mixing vessel is passed towards a point of use and to dilute the liquid downstream of the mixing vessel.

[0131] Dilution can be effected by feeding liquid from the mixing vessel into a water conducting line, the mixing vessel liquid being pumped at a known rate and the diluted liquid being pumped at a higher known rate, whereby water is drawn from a source at a flow rate being the difference between the known flow rate of the mixing vessel liquid rate and the known flow rate of the diluted liquid. Thus, the extent of dilution will be known. In order to be sure to obtain the correct formulation for the diluted liquid, having regard to its medical use e.g. as peritoneal dialysis fluid, it is also ensured that the extent of dilution is correct. This may be achieved by providing a suitable measuring means, such as conductivity measuring means. The cost, size and weight of the apparatus may be minimised by measuring the concentration of the concentrates in the diluted liquid downstream of the mixing vessel using the same measuring means as is used to

measure the concentration of the concentrates during delivery to the mixing vessel.

[0132] Where a common flow path is used at some point downstream of the valve associated with each concentrate, it may be desirable to flush that path (or part thereof) after delivery of one concentrate and before delivery of the next. In one arrangement, the pump is reversible and connectable to a source of liquid, such that in use of the apparatus, after termination of delivery of a the concentrate, the pump is reversed to pump the liquid from the source thereof through the associated flow regulator so as to flush the path between the liquid source and the flow regulator, such as a valve. The liquid used for flushing is preferably water.

[0133] It will be appreciated from the foregoing that the system for producing different medical formulations at a treatment location involves a further inventive aspect. A fifth aspect of the present invention is therefore concerned with such a system.

[0134] In one form of the fifth aspect, the present invention provides apparatus for use at a treatment location which uses a plurality of concentrates and is able to produce from those concentrates a range of different peritoneal dialysis fluid formulations, each such formulation being based on predetermined prescription information and comprising at least one of the concentrates in diluted form.

[0135] Such an apparatus is an advance over the known systems for peritoneal dialysis involving the use of a range of pre-prepared formulations, which are made remotely from the treatment location and must then be selected according to the required formulation and transported to the treatment location. Rather, the plurality of concentrates is used by the apparatus to make up the required formulation on site, according to prescription information determined by a physician or other qualified medical professional. This simplifies inventory control for the manufacturer, who no longer has to produce a range of different pre-prepared

formulations, but instead can supply the plurality of concentrates. This is also more convenient for the physician and the patient, who no longer need to concern themselves with ensuring that they are supplied with the right pre-prepared bags of fluid.

[0136] In another form of the fifth aspect, the present invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising: a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid; a fluid mixer arranged to mix the concentrates with liquid to produce peritoneal dialysis fluid;

a controller arranged to control the fluid mixer selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other;

a sterilizer arranged to sterilize at least one of the liquid and the peritoneal dialysis fluid; and

a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal cavity of a patient; and further wherein

the controller has data input means for receiving predetermined prescription information for a patient and the controller is operable to control the fluid mixer to produce a peritoneal dialysis fluid formulation based on the received predetermined prescription information.

[0137] Thus, the plurality of concentrates can be used to make the formulation required by a patient and based on a prescription determined in advance of treatment. There is no need to use a different set of concentrates for each formulation, and accordingly no need to have a required set of concentrates delivered to the treatment location. The prescribing process is separated from the delivery process, giving medical practitioners greater freedom to vary a prescription e.g. from one treatment to the next. Because of the greater flexibility in prescribing which is provided, it

may be possible to keep some patients on peritoneal dialysis treatment for longer before they have to be switched to hemodialysis treatments.

[0138] In one embodiment, the chambers are in the form of compartments of a container and all the concentrates required to make a the peritoneal dialysis formulation are provided in the compartments. Thus, a single container of concentrates can be used to make a range of different formulations, again simplifying use of the system for medical practitioners and for patients.

[0139] The concentrates may comprise a plurality of electrolytes and the controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative electrolyte concentrations from each other. Thus, a medical practitioner can vary the relative electrolyte concentrations to take account of a patient's surplus or shortage of certain salts or ions. Again, this can be done without concern for what pre-prepared bag or bags of formulations are available for use at the treatment location.

[0140] In a further form of the fifth aspect, the present invention provides apparatus for the production of peritoneal dialysis fluid at a treatment location for introduction into the peritoneal cavity of a patient, the apparatus comprising:
a plurality of chambers each containing a respective concentrate of a constituent of the peritoneal dialysis fluid;
a fluid mixer arranged to mix the concentrates with liquid to produce the peritoneal dialysis fluid;
a controller arranged to control the fluid mixer selectively to produce peritoneal dialysis fluids chosen from a group of formulations which are different from each other;
a sterilizer arranged to sterilize at least one of the liquid and the peritoneal dialysis fluid; and
a patient fill connection arranged to fluidly communicate the peritoneal dialysis fluid to the peritoneal dialysis of a patient; and further wherein
the concentrates comprise a plurality of electrolytes, and the

controller is operable selectively to produce peritoneal dialysis fluid formulations having different relative concentrations of electrolytes.

[0141] The advantages of such apparatus will be apparent from the discussions above and below.

[0142] It is to be understood that both the foregoing general description and the following detailed description are exemplary and are intended to provide further explanation of, without limiting the scope of, the invention as claimed.

BRIEF DESCRIPTION OF THE DRAWINGS

[0143] Embodiments of the present invention will now be described by way of example only, and with reference to the following detailed description which, in turn, refers to the accompanying drawings, in which:

[0144] Figure 1 is a front, perspective, partially schematic view of an apparatus for the preparation of peritoneal dialysis fluid according to one embodiment of the present invention;

[0145] Figure 1a is a block diagram of a processor system in the apparatus of figure 1;

[0146] Figure 2 is a schematic representation of a fluid path in the apparatus of Figure 1, in terms of interconnected functional modules;

[0147] Figure 3 is a detailed schematic representation of a water preparation module of Figure 2;

[0148] Figure 4 is a detailed schematic representation of a thermal control and sterilization module of Figure 2;

[0149] Figure 4a is a detailed schematic representation of an alternative embodiment of the thermal control and sterilization module of Figure 4;

[0150] Figure 5 is a detailed schematic representation of a concentrate mixing module of Figure 2;

[0151] Figure 5a is a detailed schematic representation of an alternative embodiment of the concentrate mixing module of Figure 2;

[0152] Figure 5b is a detailed schematic representation of

an alternative embodiment of the concentrate mixing module of Figure 5a;

[0153] Figure 6 is a detailed schematic representation of a drainage module of Figure 2;

[0154] Figure 7 is a detailed schematic representation of a cyclor and sterilizable connector module of Figure 2;

[0155] Figure 8 is a front perspective representation of a first example of a heat exchanger for use in the sterilizing of PD fluid according to the present invention;

[0156] Figure 9 is a front, perspective view of a second embodiment of a heat exchanger for use in the sterilizing of PD fluid according to the present invention;

[0157] Figure 10 is a side, perspective view of a disposable concentrate container according to the present invention;

[0158] Figure 11 is a side, elevational, partially sectional view through the disposable concentrate container of Figure 10 with a vertical section of a chassis removed;

[0159] Figure 12a is a side, perspective view of a portion of the disposable concentrate container of Figure 10;

[0160] Figure 12b is a bottom, perspective view of another portion of the disposable concentrate container of Figure 10;

[0161] Figure 12c is a top, perspective view of another portion of the disposable concentrate container of Figure 10;

[0162] Figure 13 is a front, perspective view of a compartment of the disposable concentrate container of Figure 10;

[0163] Figure 14 is a front, perspective view of a further compartment of the disposable concentrate container of Figure 10;

[0164] Figure 15 is a side, elevational, sectional view through the disposable concentrate container of Figure 10 during fitting to the apparatus of the present invention;

[0165] Figure 16 is a side, elevational, exploded, sectional view through the disposable concentrate container of

Figure 10 during fitting to the apparatus of the present invention;

[0166] Figure 17 is a side, elevational, sectional view through the disposable concentrate container of Figure 10 in position on the apparatus of the present invention;

[0167] Figure 18 is a side, elevational, sectional view of an alternative embodiment of the disposable concentrate container of Figure 10;

[0168] Figure 19a is a side, elevational, schematic view of a sterilizable connector of the apparatus of the present invention;

[0169] Figure 19b is a side, elevational, sectional view of a sterilizable connector of the apparatus of the present invention;

[0170] Figure 19c is a side, elevational, sectional view of a sterilizable connector of the apparatus of the present invention;

[0171] Figure 19d is a side, elevational, sectional view of a sterilizable connector of the apparatus of the present invention;

[0172] Figure 20 is a top, elevational, schematic view of a disposable fluid line for use with the apparatus of the present invention;

[0173] Figure 21 is a top, elevational, schematic view of a sampling disposable fluid line for use with the apparatus of the present invention;

[0174] Figure 22 is a side, elevational, partial, sectional view of a compartment of the disposable concentrate container of Figure 10;

[0175] Figure 23 is a side, elevational, sectional view through a glucose compartment of the disposable concentrate container of Figure 10.

[0176] Figure 24 is a side, elevational, sectional view through a lactic acid compartment of the disposable concentrate container of Figure 10; and

[0177] Figure 25 is a side, elevational, sectional view

through the lactic acid compartment of Figure 24 in an engaged position.

DETAILED DESCRIPTION

[0178] Referring to the Figures, in which like reference numerals refer to like elements thereof, Figure 1 is a partially schematic perspective view of an apparatus 100 for the preparation of peritoneal dialysis fluid for a patient according to a first embodiment of the present invention. The apparatus 100 is connected to a domestic water supply by means of a tap water connection 1 and is connected to the domestic sewerage system by means of an external drain connection 16. The external waste connection 16 may be in the form of a replaceable waste line. The apparatus 100 is powered by the domestic electricity supply by means of a mains electricity connection 20. Concentrated components of the PD fluid are supplied to the apparatus 100 in a concentrate disposable container 402. The PD fluid is supplied to and drained from the patient's peritoneal cavity by a disposable fluid line 10 which forms a fluid connection between the patient and the apparatus 100.

[0179] The apparatus 100 receives details of a prescription of the PD fluid for the patient on a smart card 102 which is read by the apparatus 100. The apparatus 100 also includes a control panel 104 which displays information to the patient and allows the patient to control the operation of the apparatus in certain respects.

[0180] In overview, the apparatus 100 according to this embodiment of the present invention is installed in a patient's home and purifies tap water from the tap water connection 1, mixes the purified tap water with concentrated PD fluid components from the concentrate disposable container 402 to produce PD fluid. The apparatus 100 then sterilizes the PD fluid and delivers the PD fluid by way of the disposable fluid line 10 directly to the peritoneal cavity of the patient. During a treatment session, which comprises a series of fill and drain cycles, old PD fluid, dialysate, is removed

and fresh PD fluid is added to the patient's peritoneal cavity, normally during the night while the patient is asleep.

[0181] The disposable container 402 may include a bar code 18 arranged on the container at a convenient position. A bar code reader 19 shown in broken lines, inside the apparatus 100 reads the bar code as the container is inserted in the apparatus.

[0182] Although the apparatus 100 is primarily intended for use in a patient's home, the apparatus 100 may be used in centers such as dialysis clinics and hospitals. The apparatus includes a control system (not shown) which monitors and controls the operation of the apparatus 100 during normal use. In addition to the control system, the apparatus 100 includes a protective system (not shown) which is separate from the control system and monitors the correct operation of the apparatus 100 independently of the control system to ensure that the patient's safety is not compromised. The control system and the protective system are able to carry out functional tests to ensure that they are operating correctly.

[0183] At the start of the treatment session, the user, for example the patient, is required to confirm some of the parameters of the intended treatment which are displayed on the control panel 104. Such parameters include, for example, the patient's name, the volume of PD fluid to be entered into the peritoneal cavity of the patient, the glucose concentration of the PD fluid or the expiration date of the disposable concentrate container 402. Some of these parameters are stored on the smartcard 102. This corresponds to the stage in traditional PD treatments where the patient compares the label on the plastic bag of PD fluid with the instructions given by the doctor. Also, at the start of the PD treatment, the patient is required to identify himself to ensure that the apparatus is not operated by an unauthorised person.

[0184] At the end of a treatment session, the concentrate disposable container 402 is replaced and the old container is discarded. Similarly, the disposable fluid line 10 is also

replaced at the end of the treatment session with a new line.

[0185] At the start of a treatment session, the patient can set the concentration of glucose required in the PD fluid for that treatment session, within predefined limits, according to the patient's requirements. The glucose concentration is set by the patient using the control panel 104. The glucose in the PD fluid acts as an osmotic agent, so that an increase in the glucose concentration will result in an increase in the volume of fluid drawn across the peritoneum of the patient during the PD treatment.

[0186] The apparatus 100 is suitable for continuous cycling peritoneal dialysis (CCPD), where the peritoneal cavity is filled and emptied of PD fluid in a cyclic sequence, usually during the night. The apparatus 100 is also capable of carrying out tidal peritoneal dialysis according to which the peritoneal cavity is initially filled with PD fluid and in subsequent cycles a volume less than the total volume of the initial fill is drained from the peritoneal cavity and replaced with an approximately equal volume of fresh fluid. The peritoneal dialysis treatment session may take place while the patient is asleep and thus the apparatus 100 is usually located adjacent the patient's bed. Other treatment modes are also possible.

[0187] At the end of a treatment session, the peritoneal cavity of the patient may be left full of PD fluid or the PD fluid may be drained from the peritoneal cavity, depending on the patient requirements. In general, it is expected that the apparatus 100 will be the sole source of the patient's PD treatment. Thus, if at the end of a treatment session the patient's peritoneal cavity is full of PD fluid, it is expected that the cavity will be full of PD fluid at the beginning of the next treatment session. However, the patient may have drained or filled his peritoneal cavity manually using additional PD equipment between treatment sessions. The apparatus 100 is able to respond to such situations by having input means whereby the patient may enter relevant data to the

apparatus.

[0188] In a usual treatment session, a total volume of about 8-25 litres of PD fluid is put into and removed from the patient's peritoneal cavity, with each fill volume being between 250 ml and 3 litres (the smaller volume may be in the case of tidal peritoneal dialysis, for example). One treatment session may involve up to 20 fill and drain cycles, with a maximum of 25 litres of PD fluid (50 litres if the disposable concentrate container 402 is changed) being supplied to the patient and a maximum of 35 litres of fluid (per container used) being drained from the patient, the drain volume being up to 4 litres per cycle.

[0189] The patient is able to instruct the apparatus 100 by means of the control panel 104 to abandon the treatment session and allow the patient to disconnect from the apparatus 100 or to finish the treatment session early by omitting some of the cycles within the treatment session.

[0190] The apparatus 100 includes a timer (not shown) which allows the patient to set the approximate time at which a treatment session should begin so that the apparatus 100 can make the necessary preparations for the treatment session before the patient arrives. Thus, when such a time has been set, treatment can begin less than 20 minutes, preferably less than 10 minutes, after the patient has arrived and has confirmed that a treatment session is actually required. If the timer has not been preset, the apparatus 100 may require up to one hour to make the necessary preparations for the delivery of dialysis fluid.

[0191] The control panel 104 includes a 256 colour video touch screen display with a screen saver. The control panel allows the user, *inter alia*, to set the glucose level concentration of the PD fluid within preset limits, start, interrupt, resume, abandon or finish the treatment session, adjust the temperature of the dialysis fluid between 35°C and 40°C and set the planned start time for the next or subsequent treatment sessions. The control panel displays the treatment

status and the time until the end of the treatment session during treatment or the time until the start of the treatment session during preparation for a treatment session. On request, the control panel 104 displays the treatment mode (for example tidal or continuous peritoneal dialysis), the number of cycles in the treatment session, the glucose concentration, the accumulated fill volume for the treatment session, the accumulated drain volume for the treatment session, the accumulated ultrafiltration volume for the treatment session, the fluid delivery temperature set point, patient identification information from the smartcard 102 or patient entered information, the status of the treatment session and technical error codes. The ultrafiltration volume is the difference between the volume of PD fluid supplied to the patient and the volume of PD fluid drained from the patient. The control panel is also able to display visual alarms and is provided with an audible alarm with which the apparatus 100 can bring the patient's attention to operating problems. The control panel 104 may also be arranged to display additional information for use by a nurse, such as service information and fill rates and volumes, provided that the nurse can provide a valid identification code.

[0192] The apparatus 100 can be interrogated by a service engineer using a laptop computer (not shown) either directly or via a remote connections such as a modem (not shown).

[0193] The smartcard 102 stores the patient's prescription and for each of the last 20 treatment sessions, the prescription, the ultrafiltration volume, the monitor identity, date and time plus any variances between the prescribed and delivered treatment and the reasons therefor if known to the monitor. The smartcard 102 also stores patient identification information and the acceptable limits of patient-selected levels such as numbers of cycles and glucose concentration. The physical characteristics of the smartcard are similar to those used in the PD 200™ peritoneal dialysis system manufactured by Gambro AB of Lund, Sweden, although the

apparatus 100 can differentiate between the PD 200 cards and cards suitable for use with the apparatus 100.

[0194] The information on the smartcard 102 can be altered by a doctor either by connecting a computer (not shown) with a suitable interface to the apparatus 100 or by inserting the smartcard 102 into a suitable card reader attached to a computer (not shown). Service personnel are also able to interrogate the apparatus 100 using a computer (not shown) and a data link directly to the apparatus.

[0195] Figure 1a shows a block diagram of a smart card reader 103 which is connected to an operating system processor 108 and a protective system processor 106. The processors operate and supervise the system in a manner previously known in the art of dialysis machines. The processors are also connected to the control panel 104. Processors 106 and 108 are associated with memory devices 110 and 112, such as volatile memory, static memory, hard disk, solid state memory devices etc.

[0196] The operating system processor receives data input from sensors and other means in the apparatus and output control signals for controlling processes in the apparatus such as valves and pumps.

[0197] The protective system processor receives data input from sensors and other means in the apparatus and output control signals for the purpose of supervising the operating system processor and other processes in the apparatus. The protective system sensors are separate from the operating system processor sensors.

[0198] Figure 2 shows schematically the fluid path in the apparatus 100 of Figure 1. The apparatus is, for ease of understanding, represented in terms of six interconnected functional modules, which each perform a specific role in the preparation of the peritoneal dialysis fluid and the peritoneal dialysis treatment. These modules are: a water preparation module 200; a thermal control and sterilization module 300; a concentrate mixing module 400; a drainage module

500; a cyclor and sterilizable connector module 600; and a sampling module 700.

[0199] In the following, the overall structure of the fluid path in the apparatus 100 will be described and then further details of the individual modules will be given.

[0200] As used in this description the terms "cleaning", "disinfection" and "sterilization" have distinct meanings: "cleaning" simply means the removal of deposits within the system; "disinfection" means the neutralisation of most bacteria; and "sterilization" means the inactivation of all bacteria with a 1 in 10^6 confidence level, i.e. the theoretical probability of the presence of a viable microorganism is less than or equal to 10^{-6} (see United States Pharmacopoeia, 23rd Edition and European Pharmacopoeia 1997).

[0201] As shown in Figure 2, tap water from the domestic supply is provided to the water preparation module 200 by means of the tap water connection 1. The water preparation module 200 controls the supply of water to the other modules in the apparatus by switching the tap water supply on and off, by limiting the pressure of the water supply and by monitoring the availability of the water supply. The water preparation module 200 also reduces and controls the level of dissolved gas and chemical and bacteriological contamination in the water supplied to the concentrate mixing module 400. The water preparation module 200 is capable of operating with potable water as generally defined by the US Environmental Protection Agency in the drinking water standard of November 1996, at pressures from 1-6 bar gauge (100-600 kPa above atmospheric pressure) and at temperatures between 5 and 30°C.

[0202] The water preparation module 200 is connected to the thermal control and sterilization module 300 by means of five fluid connections 2a-2e. A cooling water output connection 2a supplies softened, pressure-controlled water for use in the cooling functions of the thermal control and sterilization module 300. The temperature of the cooling water is raised in the thermal control and sterilization module 300, due, at

least in part, to the water being used for cooling purposes. In this way, the water returned to the water preparation module 200 is preheated to improve the efficiency of the water preparation module, using waste heat from other parts of the apparatus 100. The cooling water is returned to the water preparation module 200 from the thermal control and sterilization module 300 through a cooling water return connection 2b at a controlled temperature of approximately 30°C.

[0203] Purified water prepared by the water preparation module 200 is passed to the thermal control and sterilization module 300 by means of a purified water connection 2c. Waste water from the water purification process is passed from the water preparation module 200 to the thermal control and sterilization module 300 for cooling by means of a purification waste connection 2d.

[0204] The water preparation module 200 vents excess gas to atmosphere through an isolator air vent 17. The water preparation module 200 is also able to vent air to and from the thermal control and sterilization module 300 through a patient heat exchanger vent connection 2e.

[0205] For disinfection purposes the water preparation module 200 receives water at disinfection temperature from the concentrate mixing module 400 by means of a reverse osmosis (RO) membrane disinfection connection 3.

[0206] The water preparation module 200 has a connection for a disinfectant cartridge 210, which supplies chemical disinfectant for the disinfection of the water preparation module 200, when required.

[0207] The thermal control and sterilization module 300 sterilizes the PD fluid supplied to the patient, and provides a supply of sufficiently hot water for disinfection of the concentrate mixing module 400 and the drainage module 500.

[0208] The thermal control and sterilization module 300 also controls the temperature of the water supplied to the water preparation module 200 by means of the cooling water

return connection 2b and to the concentrate mixing module 400 by means of a mixing water feed connection 4a. One important role of the thermal control and sterilization module 300 is to prevent heat being wasted and to sequence heating operations, so that the apparatus does not require more power than can be supplied by a domestic electricity socket. The apparatus 100 is designed to operate with a mains electricity supply of either 90-140V, 10A, 50/60 Hz (for example in North America and Japan) or 198-253V, 10A, 50/60 Hz (for example in Europe). The maximum power consumption of the apparatus 100 is therefore between 0.9 kW and 2.5 kW. During filling of the patient with PD fluid, the power consumption is around 1.2 kW. If the electricity supply is unable to provide sufficient power to sterilize the PD fluid at a flow rate of 300 ml/min, the flow rate is reduced, for example to 150 ml/min, to reduce the power required to sterilize the PD fluid. The major part of the energy consumption of the apparatus 100 is required for heating of water and PD fluid for disinfection and sterilization during filling of the patient.

[0209] The connections between the water preparation module 200 and the thermal control and sterilization module 300 are described above. The thermal control and sterilization module 300 also supplies temperature controlled purified water to the concentrate mixing module 400 via the mixing water feed connection 4a. The output, for example PD fluid, of the concentrate mixing module 400 is returned to the thermal control and sterilization module 300 by means of a mixing module output connection 4b.

[0210] The fluid entering the thermal control and sterilization module 300 at the mixing module output connection 4b passes through an input volumetric flow meter 350 which, when the apparatus is supplying PD fluid to the patient, measures the volume of fluid supplied to the patient. An output volumetric flow meter 650 is provided in the cyclor and sterilizable connector module 600 and measures the volume of fluid removed from the patient. The change in the patient's

body fluid level due to the PD treatment is calculated by subtracting the volume of fluid drained from the patient from the volume of fluid supplied to the patient. This change is called the ultrafiltration volume (UF) and is measured in the range -4 litres to +10 litres over the treatment session to an accuracy of ± 66 ml (or 0.66% of the total fill volume, if greater), preferably ± 33 ml (or 0.33% of the total fill volume, if greater).

[0211] When treating the patient, sterile PD fluid is passed from the thermal control and sterilization module 300 to the cycler and sterilizable connector module 600 via a sterile fluid connection 8a. During sterilization of the cycler and sterilizable connector module 600, water at sterilization temperature is passed from the thermal control and sterilization module 300 to the cycler and sterilizable connector module 600 by means of the sterile fluid connection 8a and returned to the thermal control and sterilization module 300 by means of a sterilization output connection 8b. The sterilization water is returned to the cycler and sterilizable connector module 600 after heat recovery by the thermal control and sterilization module 300 by means of a sterilization fluid return connection 8c.

[0212] The thermal control and sterilization module 300 connects to the drainage module 500 by means of a thermal drain connection 13a, which is used to pass the waste water from the purification waste connection 2d to the drainage module 500 after heat recovery. During disinfection, fluid is passed at low pressure from the drainage module 500 to the thermal control and sterilization module 300 for heat recovery by means of a heat recovery drain connection 13b. This fluid is returned to the drainage module 500 after heat recovery by means of a heat recovery drain return connection 13c.

[0213] The concentrate mixing module 400 mixes concentrated PD fluid to the required recipe and supplies the PD fluid, suitably diluted, to the thermal control and sterilization module 300 for sterilization. The concentrate mixing module

400 also supplies cleaning agent to downstream modules of the apparatus, and controls the venting of air from the fluid circuit, while keeping microbiological contamination to a minimum.

[0214] As explained above, purified water is supplied to the concentrate mixing module 400 by means of the mixing water feed connection 4a from the thermal control and sterilization module 300, and chemically controlled PD fluid is returned to the thermal control and sterilization module 300 via the mixing module output connection 4b. The concentrate mixing module 400 also has an air vent connection 6 to atmosphere to allow filling and draining of the fluid system, and a mixing module drain connection 15, which is used to supply water at disinfection temperature to the drainage module 500. Water at disinfection temperature is also supplied to the water preparation module 200 by means of the RO membrane disinfection connection 3.

[0215] The PD fluid is prepared by the concentrate mixing module 400 from concentrated components of the PD fluid provided in a disposable concentrate container 402 which connects to a manifold 404 of the concentrate mixing module 400 and is enclosed by a manifold cap 406.

[0216] Turning now to the drainage module 500, this module controls the flow of fluid to the external waste connection 16 and provides the negative pressure required to drain the patient of dialysate (the fluid removed from the patient at the end of a PD treatment). The external waste connection 16 may be permanently connected to the domestic sewerage system or temporarily connected, for example clipped over a lavatory bowl. The drainage module 500 also closes the drain line to isolate the fluid system when necessary, and stops the flow from the water preparation module to allow disinfection. The maximum flow rate to the external waste connection 16 is 3 litres/min and the maximum temperature of the fluid passing through the external waste connection 16 is 85°C.

[0217] The majority of the connections to the drainage

module 500 have been described in relation to the other modules of the apparatus. The remaining connections, to the cyclor and sterilizable connector module 600, will be described below.

[0218] The cyclor and sterilizable connector module 600 prevents PD fluid of unsafe chemical composition, temperature or pressure or non-sterile PD fluid from being passed to the patient 50, by closing off the appropriate supply lines. As described above, the cyclor and sterilizable connector module 600 is connected to the thermal control and sterilization module 300 by means of the sterile fluid connection 8a, the sterilization output connection 8b and the sterilization fluid return connection 8c. The cyclor and sterilizable connector module 600 connects to the patient 50 by means of a patient fill connection 9a and a patient drain connection 9b. The patient connections, 9a and 9b, are made to a disposable fluid line 10 which is replaced by the patient 50 at the start of each PD treatment session and connects to the standard connector on the catheter (not shown) into the patient's peritoneal cavity. The disposable fluid line 10 is provided to the patient pre-sterilized and in a sterile package. The disposable fluid line 10, which may be seen in Fig. 19, 20 and 21, has a pierceable membrane 634 at the end that connects to the cyclor and sterilizable connector module 600 and this membrane 634, in combination with a cap (not shown) on the catheter connector 654, maintains the sterility of the disposable fluid line 10 until it is used.

[0219] The cyclor and sterilizable connector module 600 is arranged such that the fluid circuit from the sterile fluid connection 8a to the sterilization output connection 8b which includes the pierceable membrane 634 at the end of the disposable fluid line 10 can be heat sterilized with water at sterilization temperature from the thermal control and sterilization module 300. The cyclor and sterilizable connector module 600 maintains the sterility of the fluid circuit once the membrane 634 on the fluid line 10 has been

pierced until the end of the treatment session, and also ensures that fluid can only be passed to the patient when intended.

[0220] The cycler and sterilizable connector module 600 has a negative pressure drain connection 14a to the drainage module 500 for draining the dialysate from the peritoneal cavity of the patient, and an ambient pressure drain connection 14b which is used to drain fluids other than the dialysate from the cycler and sterilizable connector module 600.

[0221] The sampling module 700 is connected to the disposable fluid line 10 via sampling interface 11 and collects a 15 ml sample of dialysate, when requested, for analysis. The sample represents an average of the composition of the drained dialysate over all the cycles of the treatment session.

[0222] The structure of the individual modules will now be described in more detail with reference to the figures.

[0223] Water Preparation Module 200

[0224] Figure 3 shows in detail the structure of the water preparation module 200. Tap water from the domestic mains supply enters the water preparation module 200 through the tap water connection 1. The flow of mains water can be switched off completely by an inlet valve 202. From the inlet valve 202, the water passes through a 30 micron particulate filter 204 which protects the moving parts of the water preparation module 200 from coarse particles in the water supply. The filter 204 also prevents damage or blocking of the downstream components of water preparation module 200, such as reverse osmosis membranes or particle filters.

[0225] The filtered water passes through a water softener 206, for example in the form of an ion exchange column. Waste water from the water softener 206 produced during regeneration of the water softener 206 is passed to the drainage module 500 by means of a normally closed water softener valve 268, the purification waste connection 2d and the thermal drain

connection 13a of the thermal control and sterilization module 300. The water softener 206 protects the fluid components of the water preparation module 200, such as reverse osmosis (RO) membranes, 238 and 252, from lime scale which would degrade their performance. It is important for the operation of the RO membranes, 238 and 252, that the supplied water is soft in order to prevent a build-up of lime scale.

[0226] The softened water passes to an isolator 208, in the form of a tank equipped with a float valve, which prevents a back flow of material from the water preparation module 200 into the mains supply and also reduces the pressure of the water from mains pressure to atmospheric pressure. Air from the isolator 208 is directed to atmosphere at the isolator air vent 17, which can be opened and closed by an isolator air vent valve 209. The isolator 208 is also able to receive air from and pass air to the thermal control and sterilization module 300 by means of the patient heat exchanger vent connection 2e.

[0227] Downstream of the isolator 208, a branch of the fluid path including the disinfection cartridge 210 connects to the main fluid path and will be described later. The softened water in the main fluid path passes from the isolator 208 to the thermal control and sterilization module 300 by means of the cooling water output 2a and is used in the thermal control and sterilization module 300 for cooling purposes and pre-heating before being returned to the water preparation module 200 by means of the cooling water return connection 2b at a controlled temperature of approximately 30°C. The raised temperature of the water due to the preheating in the thermal control and sterilization module 300 reduces the power required to pump the water through the RO membranes and improves the effectiveness of the degassing operation described below.

[0228] The preheated water returning to the water preparation module 200, by means of the cooling water return connection 2b passes through a series of components, 214

through 224, which remove dissolved gas from the water. These components are a proportioning valve 214, a degassing restrictor 216, an expansion chamber 218, a degassing pump 222 and a degassing chamber 224. In operation, water from the degassing chamber 224 is recirculated by means of the proportioning valve 214 through the degassing restrictor 216 by the degassing pump 222, which is a gear pump. The pressure drop in the water due to the degassing restrictor 216 causes dissolved gas in the water to be forced out of solution and begin to form bubbles in the water. The pressure drop due to the degassing restrictor 216 is a function of the flow rate there through, which is maintained constant by recirculation from the degassing chamber 224, at a flow rate set by the degassing pump 222.

[0229] The degassing chamber 224 includes a level sensor 225, such as an ultrasonic level sensor, which detects the level of the water in the degassing chamber 224. The level sensor 225 controls the operation of the proportioning valve 214 such that if the level of water in the degassing chamber 224 drops, the proportioning valve 214 is adjusted to allow water from the cooling water return connection 2b to supplement the water recirculated by the degassing pump 222 until the water level in the degassing chamber 224 returns to the maximum level. The recirculated flow from the degassing chamber 224 is decreased to maintain the flow through the degassing restrictor 216 constant. In this way, any flow of water out of the degassing chamber 224 downstream towards the RO membranes 238,252 is replaced by a flow of water at the same rate from the cooling water return connection 2b. However, the flow rate through the degassing restrictor 216 remains constant regardless of the downstream flow rate from the degassing chamber 224 due to the operation of the proportioning valve 214. A constant flow of 900 ml/min through the degassing restrictor 216 gives a pressure drop of 800 mbar (80 kPa), which is sufficient for effective degassing.

[0230] The reduced pressure water passes from the degassing

restrictor 216 to the expansion chamber 218 which slows the flow sufficiently that bubbles of gas initiated during the rapid pressure reduction in the restrictor combine and have time to increase in size. Some of the bubbles rise to the surface of the water in the expansion chamber 218 and form a small head space of gas in the expansion chamber 218. The expansion chamber is provided with a gas-pipe 219 which connects the headspace in the expansion chamber 218 to the fluid path between the expansion chamber 218 and the degassing pump 222, so that gas bubbles are entrained in the fluid drawn from the expansion chamber 218 by the degassing pump 222. The mixture of gas and water are drawn from the expansion chamber 218 by the degassing pump 222 and the pressure of the water is monitored by a degassing pressure sensor 220 to ensure that the pressure is sufficiently low for effective degassing. The degassing pump 222 pumps the gas and water into the degassing chamber 224 where the gas is vented to the isolator 208 at atmospheric pressure. The level sensor 225 in the degassing chamber 224 controls the fluid flow through the proportioning valve 214 as described above by opening the proportioning valve 214 to increase the proportion of the flow through the degassing restrictor 216 directly from the cooling water return connection 2b when the water level drops due to water being drawn from the degassing chamber 224 by downstream components of the water preparation module 200. In this way, fluid continuity in the subsequent sections of the water preparation module 200 is ensured.

[0231] A bypass from upstream of the proportioning valve 214 directly to the degassing pressure sensor 220 under the control of a degassing bypass valve 226 is provided so that disinfection can take place without the pressure drop associated with the degassing restrictor 216.

[0232] The degassed water from the degassing chamber 224 is drawn by an RO pump 236 (Model Procon 1608, from Procon Products Div./Roehlen Industries, Ten, USA) through an incoming water conductivity meter 228 which, in combination

with an incoming water temperature sensor 230, measures the conductivity of the water. Each conductivity measurement of the water (or the PD fluid) by the apparatus 100 of the invention is accompanied by a temperature measurement, as the measured conductivity of a solution varies with temperature. The conductivity measurements are compensated by reference to the temperature at which they are taken to provide an indication of the ionic concentration in the water (or PD fluid).

[0233] After the conductivity measurement, the water passes through an activated carbon filter 232, available from Gambro AB of Lund, Sweden as part No. K06735001, the purpose of which is to remove free chlorine from the water and to adsorb some organic contaminants. Chlorine in the water can damage the surface of the membranes of the RO membrane units, 238 and 252.

[0234] Following the activated carbon filter 232 the water passes through a 5 micron particulate filter 234 which removes from the water any traces of carbon or other particulate matter not caught by the first filter 204 which could foul the RO membranes in units, 238 and 252.

[0235] The filtered water is pumped by the high pressure RO pump 236, preferably a rotary vane pump, past the surface of a first membrane in a RO membrane unit 238 (Type HSRO/2521/FF from Dow Film Tech, USA) and through a first RO output restrictor 240 to the drainage module 500 by means of the purification waste connection 2d and the thermal control and sterilization module 300. The high pressure of the water passing over the surface of the membrane in the first RO membrane unit 238 causes some of the water to pass through the membrane in RO membrane unit 238 overcoming the osmotic counterpressure caused by the ions in the retained liquid, in a reverse osmosis process. The remaining water, which includes any impurities which were present in the water, passes through the first RO output restrictor 240 to the purification waste connection 2d. The first RO output restrictor 240 maintains

the pressure across the first membrane in RO membrane unit 238 to ensure effective reverse osmosis.

[0236] A first RO differential pressure sensor 242 is provided to measure the differential pressure between the inflow to the first RO membrane unit 238 and the waste flow therefrom (before the first RO output restrictor 240), in order to detect fouling of the first RO membrane unit 238. If the membrane in RO membrane unit 238 begins to foul, the resistance of the membrane to the tangential flow between inlet and waste begins to increase. Due to the largely constant flow that is delivered from the RO pump, the pressure differential is increased. When the pressure differential increases by greater than say 0.5 Bar, which is sensed by a differential pressure sensor, 242a and 242b, the membrane is considered fouled. If the membrane in the RO membrane unit 238 begins to foul, there is also a higher pressure drop across the membrane, which is sensed by pressure sensors 242a and 242c.

[0237] The first RO differential pressure sensor 242 is in the form of two cavities separated by a diaphragm with one cavity in fluid communication with a point before the first RO membrane unit 238, as indicated by circle 242a, and one cavity in fluid communication with a point on the waste water output of the first RO membrane unit 238 before the first RO output restrictor 240, as indicated by circle 242b, or after the membrane in RO membrane unit 238, as indicated by circle 242c. The differential pressure is measured by monitoring the deformation of the diaphragm towards one or the other cavity. It is not necessary for the control system to measure the absolute pressure at the locations of the first RO differential pressure sensor 242a, as only the differential pressure is required to detect fouling of the first RO membrane in RO membrane unit 238.

[0238] The conductivity of the RO water which has passed through the first membrane in RO membrane unit 238 is measured by a first RO conductivity meter 246 in combination with a

first RO water temperature sensor 248.

[0239] A first RO membrane bypass valve 250 is provided for use in the disinfection of the water preparation module 200, and its function will be described below.

[0240] A second RO membrane unit 252 (Type HSRO/2521/FF from Dow Film Tech, USA) is provided downstream of the first RO membrane unit 238. The use of two RO membrane units, 238 and 252, gives a much higher purity of water than would be the case with only one membrane unit and also gives additional security in the event that one membrane ruptures. When measured in terms of conductivity, the first RO membrane unit 238 filters out approximately 98% of impurities from the water pumped across it by the RO pump 236, and the second RO membrane unit 252 filters out 80% of the remaining 2% of impurities. The quality of water required by the apparatus 100 is very high and may be difficult to achieve consistently with a single RO membrane. If one of the RO membranes, 238 and 252, ruptures, the other membrane will continue to provide purified water for the short period of time before the fault is detected by the protective system and the apparatus 100 is stopped.

[0241] The waste water from the second RO membrane unit 252 passes through a second RO output restrictor 254 in the same way as for the first RO membrane unit 238, except that this waste water is recycled through a disinfectant selection valve 256 back to the input of the RO pump 236. This is possible because the waste water from the second RO membrane unit 252 is already reasonably pure as it has passed through the first RO membrane unit 238. This recycling improves the overall water usage efficiency of the apparatus. Typically, in operation of the apparatus a flow rate of 750 ml/min of water is drawn from the degassing chamber 224 by the RO pump 236. This flow rate is supplemented by 250 ml/min of water recycled from the second RO membrane unit 252, so that 1000 ml/min of water is pumped towards the first RO membrane unit 238. Of this 1000 ml/min of water, 500 ml/min passes to the

purification waste connection 2d and 500 ml/min of purified water passes through the first RO membrane unit 238 to the second RO membrane unit 252. At the second RO membrane unit 252, a flow of 250 ml/min of water passes through the membrane to the purified water connection 2c and a flow of 250 ml/min is recycled back to the input of the first RO membrane unit 238.

[0242] A second RO differential pressure sensor 258 is provided to measure the differential pressure between the inflow and the waste flow of the second RO membrane unit 252 to detect fouling. The operation is the same as described in connection with the first RO differential pressure sensor 242, and the second RO differential pressure sensor 258 is divided in two cavities, a first cavity 258a and a second cavity 258b or 258c.

[0243] A RO pressure relief valve 260 is provided between the inflow to the second RO membrane unit 252 and the waste outflow therefrom, in order to control the pressure of the water presented to the second RO membrane unit 252, and to avoid a pressure build-up as the output demand at the purified water connection 2c varies. It is noted that the output demand from the second RO membrane unit 252 varies from full output, for example 250 ml/min, to zero during certain periods and anything there between. If the output from the second RO membrane unit 252 becomes small or zero, relief valve 260 shunts water in parallel to the restrictor 254 to thereby maintain approximately the same operation conditions for the first RO membrane unit 238 as with full output. This operation also reduced water consumption.

[0244] A second RO conductivity meter 262 and a second RO temperature sensor 264 are provided at the output of the second RO membrane unit 252 to measure the conductivity of the output water, in order to ensure that the water has been sufficiently purified from ionic components. An output water pressure sensor 266 is provided downstream of the second RO temperature sensor 264 to measure the pressure of the water

output via the purified water connection 2c to the thermal control and sterilization module 300.

[0245] During disinfection of the water preparation module 200, the disinfectant selection valve 256 is opened to direct the waste flow from the second RO membrane unit 252 through the disinfection cartridge 210. The disinfection cartridge 210 contains a chemical disinfectant, such as an aqueous solution of peracetic acid (a widely approved disinfectant), which is diluted by the water flow. During disinfection, a disinfection valve 212 is opened, the mains valve 202 is closed and flow through the purification waste connection 2d is prevented by the drainage module 500. The float valve of the isolator 208 prevents any backflow through the water softener 206. The first RO membrane bypass valve 250 is opened so that the waste water from the first RO membrane unit 238 is returned to the output side of the first RO membrane unit 238 rather than passing to the drainage module 500 by means of the purification waste connection 2d, which is closed by the drainage module 500. Degassing bypass valve 226 is opened to allow fluid flow there through. It will be seen therefore that a closed recirculation loop is created for circulation of the chemical disinfectant through the water preparation module 200. This closed loop disinfects most of the components and fluid paths of the water preparation module 200. However, to disinfect the fluid path between the disinfectant selection valve 256 and the RO pump 236, the disinfectant selection valve 256 is closed so that disinfection fluid already in the fluid channel between the second RO restrictor 254 and the disinfectant selection valve 256 is circulated past the disinfectant selection valve 256 and through the RO pump 236.

[0246] A further recirculation path is provided from the gas output of the degassing chamber 224 through the isolator 208 and the degassing bypass valve 226, so that disinfection fluid is able to circulate through the isolator 208. The degassing bypass valve 226 is opened to allow fluid flow there through, so that the pressure of the disinfection fluid is not

reduced by the degassing restrictor 216, which could cause the peracetic acid to form hydrogen peroxide, thereby reducing its effectiveness. Likewise, in the case of hot water disinfection, the drop in pressure through the degassing restrictor 216 could cause the water to boil. Although the degassing bypass valve 226 is opened, a small portion of the disinfection fluid is still passed through the degassing restrictor 216 to disinfect this fluid path.

[0247] Once all components downstream of the water softener 206 have been disinfected, the disinfection fluid is passed to the drainage module 500 through the purification waste connection 2d.

[0248] Water at disinfection temperature is introduced into the output side of the second RO membrane unit 252 by means of the RO membrane disinfection connection 3 for disinfection of the components of the water preparation module downstream of the second RO membrane unit 252.

[0249] In the case of heat disinfection of the water preparation module 200, the disinfectant cartridge 210 is not required and the water is heated during disinfection by the thermal control and sterilization module 200 between the cooling water output 2a and the cooling water return connection 2b.

[0250] Thermal Control and Sterilization Module 300

[0251] Figure 4 shows in detail the structure of the thermal control and sterilization module 300. Water from the cooling water output 2a of the water preparation module 200 is directed through a purification waste heat exchanger 324, where it is preheated by the water from the purification waste connection 2d passing through the purification waste heat exchanger 324 to the thermal drain connection 13a. The water heated by the purification waste heat exchanger 324 is heated by an electric water heater 322 before exiting the cooling water return connection 2b to ensure that it is at the optimum operating temperature for the water preparation module 200, normally about 30°C.

[0252] In the thermal control and sterilization module 300, water is circulated, in normal operation, by a patient output heat exchanger pump 316, in the form of a gear pump through a patient output heat exchanger 314 and a recirculation restrictor 310. The patient output heat exchanger 314 is in the form of a bath of water through which the fluid from an online autoclave 375 (described later) passes in a sealed conduit. The bath is kept at a constant temperature by the recirculating water to maintain the PD fluid passed to the patient at the required delivery temperature. If the temperature of the recirculating water is too high, a patient output heat exchanger drain valve 318 is opened so that the heated water can pass out of the patient output heat exchanger 314 to the cooling water return connection 2b via a patient output heat exchanger drain restrictor 308 and the water heater 322. A corresponding amount of colder water is drawn from the cooling water output 2a of the water preparation module 200 by the patient output heat exchanger pump 316, until the temperature of the heating bath of the patient output heat exchanger 314 has been reduced to the desired level

[0253] When it is not desired to extract heat from the patient output, for example because the patient output fluid lines are being sterilized at high temperature, the patient output heat exchanger 314 is drained under the influence of gravity by opening the patient output heat exchanger drain valve 318 and an air bleed valve 320. Air enters the patient output heat exchanger 314 through the patient output heat exchanger vent connection 2e from the isolator 208 via the opened air bleed valve 320 and an air bleed restrictor 312. When the patient output heat exchanger 314 is full of air, rather than water, negligible heat is transferred to or from the patient output fluid. In this case, the patient output heat exchanger pump 316 is inactive. The patient output heat exchanger 314 is refilled by opening the air bleed valve 320 to vent the air and reactivating the patient output heat

exchanger pump 316 with the patient output heat exchanger drain valve 318 closed.

[0254] The purified water produced by the water preparation module 200 is passed to the thermal control and sterilization module 300 via the purified water connection 2c. The purified water passes through a disinfection heat exchanger 326 which is used during disinfection of the concentrate mixing module 400 to preheat the purified water by recovering heat passing from the heat recovery drain connection 13b to the heat recovery drain return connection 13c. The preheated water exiting the disinfection heat exchanger 326 is heated to disinfection temperature by an electric disinfection heater 330. During normal operation of the apparatus, the disinfection heater 330 is used to control the temperature of the water exiting the mixing water feed connection 4a to the concentrate mixing module 400.

[0255] During disinfection of the drainage module 500, water from the purified water connection 2c bypasses the disinfection heat exchanger 326 by means of a disinfection heat exchanger bypass valve 328, so that the water exiting the heat recovery drain return connection 13c remains at the disinfection temperature of about 85°C. The disinfection heat exchanger bypass valve 328 is only used during disinfection of the drainage module 500.

[0256] The PD fluid produced by the concentrate mixing module 400 is passed to the thermal control and sterilization module 300 by means of the mixing module output connection 4b. This fluid passes through the input volumetric flow meter 350 which records the flow of PD fluid filled into the patient. The PD fluid is drawn by a gear-type, volumetric pump 352 which is monitored by a tachometer 354 to ensure that the pump is operating at the expected volume flow rate. The delivery rate of the volumetric pump 352 is also monitored independently by the input volumetric flow meter 350 to ensure correct operation. The volumetric pump 352 delivers the PD fluid at the required rate and pressure for on-line

autoclaving, i.e. 300 ml/min and 6 bar absolute (600 kPa) to prevent the fluid from boiling at 150°C. A gear type pump has been selected to ensure that the water passing through the online autoclave 375 can be pressurised by the pump to the pressure necessary for the water to be heated to sterilization temperature.

[0257] In normal operation of the apparatus 100, the PD fluid passes into the on-line autoclave (OLA) 375 through an OLA input valve 356. At this point, the pressure of the PD fluid is monitored by two independent OLA pressure sensors 358. One of the OLA pressure sensors 358 provides a pressure reading to the control system for the apparatus, the other sensor provides a reading to the separate protective system, see Figure 1a, which ensures that, even in the event of the apparatus malfunctioning, patient safety is not compromised. The pressure, temperature and conductivity sensors which are positioned to monitor parameters that are crucial to the patient's safety in the system are all duplicated in this manner, so that the patient is never endangered by a single sensor malfunction and each patient safety measurement is independently double-checked.

[0258] Downstream of the OLA pressure sensors 358 the PD fluid passes through a first OLA heat exchanger 360 and a second OLA heat exchanger 362, both of which preheat the PD fluid entering the OLA heating bath 364 by recovering heat from the fluid exiting the OLA heating bath 364. The OLA heating bath 364 is an oil heating bath heated by an electric heater 365 and provided with a recirculation pump 366 (gear pump) and a heating bath temperature sensor 368. The oil or ethylene glycol is circulated by the recirculation pump 366 through a heating fluid path 367 which includes the oil bath and the PD fluid (or water) passes through a sterilization fluid path 369. The heating fluid path 367 and the sterilization fluid path 369 are separated by a thermally conductive barrier.

[0259] In order to ensure that the liquid leaving the OLA

heating bath 364 is sterile, a parameter is defined which represents a sterilizingsterilizing value for the sterilization process and which can be calculated, for example, from an algorithm modelling the temperature distribution inside the OLA heating bath 364, and from the value of at least one other parameter which influences the sterilization treatment, namely the flow rate Q of the liquid to be sterilized in the OLA heating bath 364, the temperature (T_{in}) of the liquid to be sterilized entering the OLA heating bath 364 and the temperature (T_{Hin}) of the heating liquid (ethylene glycol) entering the OLA heating bath 364. Since the temperatures at the outlet of the OLA heating bath 364 (temperature of the sterilized liquid and temperature of the heating liquid) are linked to the temperatures at the inlet of the OLA heating bath 364, it is also possible to take into account in the calculations the temperature (T_{out}) of the sterilized liquid leaving the OLA heating bath 364 and/or the temperature (T_{Hout}) of the heating liquid leaving the OLA heating bath 364.

[0260] When the parameter representing the sterilizingsterilizing value for the treatment is defined, a set value for this parameter is then chosen which is both high enough to correspond to an effective sterilization of the liquid, and as low as possible in order to prevent or limit the degradation of the liquid to be sterilized when this liquid is heat-sensitive (as in the case of solutions for peritoneal dialysis which contain glucose).

[0261] During functioning, the control system of the apparatus 100 is programmed to calculate, at regular intervals, the value of the parameter representing the sterilizingsterilizing value for the treatment, from the algorithm of temperature distribution in the OLA heating bath 364, and the temperature and flow rate data measured by the OLA temperature sensors 370, the heating bath temperature sensor 368 and the input volumetric flow meter 350. Each time that a new value for the parameter is calculated, the control

system checks that this calculated value is higher than the set value and therefore confirms that the liquid is sterile. A further temperature sensor 379 is used for obtaining the temperature of the liquid to be sterilized by the OLA before entering the heat exchanger.

[0262] This checking process, which allows validation of the effective sterilization of the liquid, can be passive. The reason for this is that, given that the sterile state is a crucial characteristic of the PD fluid it is possible to envisage a standard operating mode for the OLA 375 in which the choice of the flow rate for the liquid to be sterilized is limited to a restricted number of different predetermined values (for example three) and in which all of the other operating parameters for the device are preset as a function of the predetermined flow rates, such that the functioning of the device is simplified as much as possible. In this case, the checking process described above is used merely to validate the sterilization.

[0263] It is also possible to envisage an operating mode for the OLA 375 in which the choice of flow rate of liquid to be sterilized is free within a range of determined values. In this case, the control system calculates, from the chosen flow rate and from the set value for the parameter representing the sterilizingsterilizing value, the other operating parameters for the device, in particular the temperature of the heating liquid as measured by temperature sensor 368. During functioning, the control system regularly adjusts the flow rate of the volumetric pump 352 and/or the temperature of the heating liquid circulated by the recirculation pump 366, such that the calculated value of the parameter is always greater than the set value.

[0264] The parameter denoted in the literature (see page 288 of the European Pharmacopoeia 1997, or page 1977 of the United States Pharmacopoeia, 23rd Edition) as F_0 (expressed in minutes) is used as the parameter representing the sterilizingsterilizing value for the sterilization process. F_0

is the sum of the cumulative sterilizingsterilizing effects during a sterilization treatment, or sterilizingsterilizing value F_0^* when the reference temperature T is equal to 250°F (121.1°C) and the thermal inactivation value Z is equal to 18°F (10°C). The thermal inactivation value Z is the temperature increase which multiplies by ten the rate of destruction of a specific microorganism. $Z = 10^\circ\text{C}$ corresponds to a theoretical microorganism which is slightly more resistant than the microorganism reputed to be more heat-resistant than any other spore-forming microorganism, *Bacillus stearothermophilus*. The canonical formula for F_0 is shown in Equation 1.

$$F_0 = \int_0^t \left(\frac{T-121}{10} \right) dt \quad (1)$$

[0265] This formula cannot be applied directly to the checking of a sterilization treatment in which the liquid to be sterilized is permanently flowing and in which the heating means used to raise the temperature of the liquid to be sterilized does not bring this liquid to the same temperature at all points in the heating chamber.

[0266] When the heating means is arranged to heat the liquid to be sterilized along a portion of the pipe in which the liquid is circulating, it is believed that the formula shown in Equation 2 can be used to calculate F_0 .

$$F_0 = \int_0^L \frac{S}{Q} \times 10^{\left(\frac{T(y)-121}{10} \right)} dy \quad (2)$$

In equation 2:

L = length of the sterilization fluid path 369 of the liquid to be sterilized through the OLA heating bath 364;

S = internal cross section of the sterilization fluid path 369 through the OLA heating bath 364;

Q = flow rate of the liquid to be sterilized through the OLA heating bath 364;

$T(y)$ = equation of the temperature distribution of the liquid

as a function of the distance from the inlet of the OLA heating bath 364.

[0267] The equation $T(y)$ depends on the structure of the OLA heating bath 364 and on its operating mode. For example, Figure 8 shows a first example of a heat exchanger which is adapted for use in the OLA 375. This exchanger consists of two concentric pipes, the outer pipe forming a sleeve around the inner pipe. The sterilization fluid path 369 is provided by the interior of the inner pipe and the heating fluid path 367 is provided between the inner and outer pipe.

[0268] During operation, the liquid to be sterilized and the heating liquid, for example ethylene glycol, are circulated, in opposite directions, in the inner pipe (sterilization fluid path 369) and in the outer pipe (heating fluid path 367). The inside diameter of the sterilization fluid path 369 is chosen such that, in the range of flow rates which includes the flow rates for operating the OLA 375 (100 to 400 ml/min), the flow of the liquid to be sterilized is always turbulent.

[0269] For an exchanger with an inner pipe made of stainless steel and an outer pipe made of copper and having the dimensions set out in Table 1 the equation for $T(y)$ can be written according to Equation 3.

Table 1

Length (cm)	222
Inner pipe volume (ml)	26
Outer pipe volume (ml)	105
Cross section of the inner pipe (cm ²)	0.117
Area of the annular space between the inner and outer pipes (cm ²)	0.502
Internal perimeter of the inner pipe (cm)	1.213
External perimeter of the inner pipe (cm)	1.995
Internal exchange area of the inner pipe (cm ²)	269
External exchange area of the inner pipe (cm ²)	443

$$T(y) = T_m + (T_{lin} - T_m) \times \frac{rx [e^{ny} - e^{nl}]}{1 - rx e^{nl}}$$

(3)

T_{in} = temperature of the liquid to be sterilized entering the sterilization fluid path 369;

T_{Hin} = temperature of the heating liquid entering the heating fluid path 367 (such as measured by the heating bath temperature sensor 368).

$$r = 6 \times 10^{-3} \times Q^2 - 0.0577 Q + 19.084$$

$$n = -\frac{1}{L} \ln \left[\frac{301415 - 958.18Q + Q^2}{292.6 + 65.72Q - 0.200453Q^3 + 0.00020948} \right]$$

Q = flow rate of the liquid in the sterilization fluid path 369.

[0270] As emerges from this example, it is possible to calculate the sterilizingsterilizing value F_0 at any moment, from a measurement of the temperature T_{in} of the liquid to be sterilized entering the OLA heating bath 364, a measurement of the temperature T_{Hin} of the heating liquid entering the OLA heating bath 364, a measurement of the flow rate Q of liquid to be sterilized and an equation modelling the temperature distribution inside the OLA heating bath 364.

[0271] In the preferred embodiment of the present invention, as shown in Figure 4, the OLA heating bath is in the form of a bath of ethylene glycol which is agitated by the recirculation of the ethylene glycol by the recirculation pump 366 to ensure a uniform temperature throughout the OLA heating bath 364. The sterilization fluid path 369 passes through the OLA heating bath 364 in a sealed conduit. The above principles are, however, applicable to the embodiment shown.

[0272] Throughout all the operating phases of the OLA 375 in which the OLA 375 is expected to produce a sterile liquid (water or PD fluid), the control system validates the sterilization treatment carried out by checking that the calculated sterilizingsterilizing value F_0 is always greater than a first threshold value F_{0min} corresponding to the sterility of the liquid.

[0273] The OLA heating bath 364 heats the PD fluid to a temperature of greater than 150°C and maintains the PD fluid at this temperature for at least 2 seconds to autoclave the PD fluid and thereby ensure sterility. The flow rate through the OLA heating bath 364 is 300 ml/min. Under these conditions it is believed that the equivalent theoretical F_0 value is at least 20 minutes.

[0274] The temperature of the sterile PD fluid exiting the OLA heating bath 364 is checked by two independent OLA temperature sensors 370 which ensure that the required temperature has been reached. Most of the heat from the autoclaved PD fluid is recovered to the PD fluid entering the OLA heating bath by the first and second OLA heat exchangers 360, 362. Any residual heat is recovered in the patient output heat exchanger 314 which ensures that the temperature is acceptable for the patient, i.e. 37°C. The temperature of the autoclaved PD fluid is checked downstream of the patient output heat exchanger 314 by two independent patient output temperature sensors 372. Finally, the pressure of the PD fluid is reduced by a patient output pressure relief valve 374 to a safe pressure for delivery to the patient. The autoclaved, pressure and temperature controlled PD fluid is then passed to the cyclor and sterilizable connector module 600 by means of the sterile fluid connection 8a.

[0275] During sterilization of the cyclor and sterilizable connector module 600 the fluid pumped by the volumetric pump 352 takes a different path through the OLA so that the fluid is at 130°C, rather than 37°C. The fluid is maintained at a pressure of 3 bar absolute (300 kPa) to prevent boiling. In this case, the fluid passes through an OLA sterilization valve 376 and through a sterilization heat exchanger 378 which recovers heat passing from the sterilization output connection 8b of the cyclor and sterilizable connector module 600 to the sterilization fluid return connection 8c. The heat recovered by the sterilization heat exchanger 378 is used to preheat the fluid, which then passes to the second OLA heat exchanger 362

for further preheating. The heating of the sterilization fluid by the OLA heating bath 364 is similar to the process for autoclaving the PD fluid. However, heat is only recovered by the second OLA heat exchanger 362 and not the first OLA heat exchanger 360 or the patient output heat exchanger 314. The patient output heat exchanger 314 has been drained at this stage so that it contains only air which is a poor conductor of heat and does not therefore transfer a significant amount of heat from the sterilization fluid. There is no flow through the heat-receiving side of the first OLA heat exchanger 360 because the OLA input valve 356 is closed and heat will not therefore be transferred to the heat-receiving side of the first OLA heat exchanger 360 once the fluid in that side has reached the temperature of the fluid in the heat transferring side. Even though there is no flow, the fluid in the heat-receiving side of the first OLA heat exchanger 360 does not boil because it is in communication with the fluid flow through the OLA heating bath 364 and is therefore at the same pressure. Thus, the fluid for sterilization which exits the sterile fluid connection 8a has a much higher temperature, 130°C, than the fluid which is provided to the patient, and is therefore suitable for sterilizingsterilizing the cyclor and sterilizable connector module 600.

[0276] The sterilization of the cyclor and sterilizable connector module 600 is considered as effective when all of the points in the fluid circuit downstream of the OLA heating bath 364 have been brought, by means of the sterile liquid, to a minimum temperature T_2 for a minimum period t_2 , which corresponds to a second set sterilizingsterilizing value F_{0min2} , given by Equation 4

$$F_{0min2} = t_2 \times 10^{\left(\frac{T_2 - 121}{10}\right)} \quad (4)$$

[0277] Validation of the sterilization of the fluid circuit can be achieved simply by the control system checking that, during an uninterrupted interval at least equal to t_2 , the temperature of the liquid measured by the patient output temperature sensors 372 has constantly been above T_2 .

[0278] Since the sterilization of the cyclor and sterilizable connector module 600 is to be carried out with sterile water, the control system must validate both the sterilization of the liquid and sterilization of the fluid circuit. In other words, the control system must check both that the sterilizingsterilizing value for the sterilization treatment applied to the liquid is greater than F_{0min1} and that the sterilizing value for the sterilization treatment applied to the circuit is greater than F_{0min2} . For this reason, the second OLA heat exchanger 362 is used, as the temperature of the sterile liquid must be brought down from the fluid sterilization temperature of 150°C (necessary to achieve F_{0min1}) to the circuit sterilization temperature of 130°C (which is lower than 150°C so that the pressure required in the cyclor and sterilizable connector module 600 is only 3 bar absolute rather than 6 bar absolute).

[0279] The patient output pressure relief valve 374 operates during sterilization to maintain the fluid before the relief valve 374 at a high pressure of 6 bar absolute and the pressure after the relief valve at the high pressure of 3 bar absolute required to prevent boiling at 130°C . A skilled person realises how to construct such a valve. If the water began to boil, it would not be possible to validate the sterilization of the circuit, since it would not be possible to certify that every point of the circuit has come into contact with water at a minimum temperature for a minimum uninterrupted period of time.

[0280] The fluid path in the apparatus 100 is carefully insulated to prevent heat loss during disinfection and/or sterilization. In particular, the relative locations of the hot components are chosen to ensure that heat loss is kept to a minimum, i.e. adjacent components keep each other warm. In this way, it is ensured that the fluid paths are maintained at the correct disinfection or sterilization temperatures along the whole of the path. A temperature sensor 380 arranged at connection 8b may be used for verifying the sterility of the

fluid circuit up to heat exchanger 378.

[0281] The heat exchangers 360,362,378 are in one embodiment shaped like the exchanger represented in Figure 9, i.e. with the junction on a part of their length of the heating pipe and the fluid pipe. The two portions of joined pipes are shaped to form a coil with joined spirals, and both the inside and the outside of the cylinder thus formed are covered with a material which is a good heat conductor.

[0282] Other details of the thermal control and sterilization module 300 are described in our co-pending application entitled "Process and device for sterilizing and dispensing a liquid for medical use", Gambro reference HP 1310, which is incorporated herein by reference and a copy of which is attached hereto.

[0283] Concentrate mixing module 400

[0284] Figure 5 shows in detail the structure of the concentrate mixing module 400. The concentrate mixing module 400 includes the disposable concentrate container 402 which interfaces with the manifold 404 and is covered by the manifold cap 406. The disposable concentrate container 402 includes chambers, in the form of compartments for an aqueous solution of lactic acid 408, cleaning agent 410 (for example powdered sodium carbonate), powdered sodium bicarbonate 412, powdered sodium chloride 414, powdered calcium chloride 416, powdered magnesium chloride 418 and powdered glucose 420. The disposable concentrate container 402 contains enough material in each compartment for a PD treatment session of the patient according to a selected one of a large number of prescriptions.

[0285] The range of composition for each of the components of the PD fluid which can be delivered to the patient stored in the disposable concentrate container 402 is set out in Table 2, together with the composition range for sodium lactate which is formed from the lactic acid and sodium bicarbonate. The mass of the components in the disposable concentrate container 402 and the approximate volume of each

compartment 408-420 are also given in Table 2.

[0286] The concentration of sodium in the PD fluid delivered to the patient is within $\pm 2.5\%$ of the requested amount. The concentration of each of the other ingredients is within $\pm 5\%$ of the requested amount. This assumes a fill volume of at least one liter. It is likely that for any given prescription, at least one of the components of the dialysis fluid in the container 402 will not be entirely used up, as the amounts are selected to cover a wide variety of prescriptions.

[0287] In addition or as an alternative to the components listed in Table 2, other components could be included, for example potassium salts.

Table 2

Component	Composition Range	Mass in compartment	Approx. volume of compartment
Sodium chloride	120-140 mmol/l	208g	300 ml
Magnesium chloride	0.25-0.50 mmol/l	36g	150 ml
Calcium chloride	1.0-2.0 mmol/l	52g	300 ml
Sodium lactate	0-40 mmol/l*	-	-
Sodium bicarbonate	0-40 mmol/l*	120g	150 ml
Lactic acid	Compatible with sodium lactate and sodium bicarbonate levels	120g	300 ml
Glucose	1.5-4.0% w/w	1176g	1800 ml
Sodium carbonate	-	20	150 ml

Note: *In any given solution, the molar concentrations of sodium lactate and sodium bicarbonate add up to between 30 and 40 mmol/l.

[0288] It should be noted that the relative arrangement i.e. the order, of the compartments, 408 through 420, in Figure 5 (and Figure 5a) is schematic only, and does not represent any physical order, but is chosen to easily represent the topology of the fluid system. Figures 10 and 11

show the order of the compartments, 408 through 420, in the disposable concentrate container 402 according to one embodiment of the invention.

[0289] Figure 10 shows the construction of the disposable concentrate container 402. The compartments, 408 through 420, are individually injection moulded in polypropylene and are mounted to a chassis 401 at their lower ends. The upper ends of the compartments, 408 through 420, are held together by a lid 403 which also serves to close off the upper end of the glucose compartment 420 and provide a carrying handle for the container 402. As is clear from Table 2, the lactic acid compartment 408, the sodium chloride compartment 414 and the calcium chloride compartment 416 are each approximately twice the volume of the cleaning agent compartment 410, the sodium bicarbonate compartment 412 or the magnesium chloride compartment 418. The glucose compartment 420 is significantly larger than the other compartments, 408 through 418. Each of the compartments, 408 through 418, is provided at its lower end with at least one connector 407 for connection to the manifold 404.

[0290] Figure 11 shows a partially sectional view through the disposable concentrate container 402 with part of the chassis 401 removed, and which clearly shows the connectors 407 of the compartments, 408 through 420. The glucose compartment 420 is provided with two connectors, 407a and 407b, the function of which will be explained below.

[0291] Figures 12a to 12c show perspective views of the lid 403 (Figure 12a), glucose compartment 420 (Figure 12b) and chassis 401 (Figure 12c) of the disposable concentrate container. As shown in Figures 12a to 12c, the lower surface of the glucose compartment 420 is sloped to direct the glucose powder in the compartment 420 towards the input connector 407a. The connectors 407 of each of the compartments, 408 through 420, are received in corresponding holes 409 defined in the chassis 401. The holes 409 are aligned in the longitudinal direction of the chassis 401 along a line A which

is offset by a distance from the longitudinal axis of symmetry B of the chassis 401. In this way, the container 402 is made rotationally asymmetric so that it cannot be inserted into the apparatus 100 the wrong way round.

[0292] The compartments, 408 through 418, are snapped in place and the glucose compartment 420 is hot riveted (heat staked) to the chassis 401 using rivets 411 which are formed integrally with the compartment 420. The rivets 411 are received in corresponding holes 405 in the chassis 401. Also, the rivets 411 of compartments 408 to 418 may be hot riveted.

[0293] The chassis 401 includes a skirt 413 which is corrugated for strength and protects the connectors 407 when the container 402 is placed on a surface. The skirt or the connectors may be provided with a removable strip 443 for the protection of the connectors 407 during transport and storage.

[0294] Figure 13 shows the magnesium chloride compartment 418 as an example of the smaller size of compartments, 410, 412, and 418. Figure 14 shows the sodium chloride compartment 414 as an example of the larger size of compartments, 408, 414, and 416. The lower surface of each size of compartments, 410, 412, and 418, and 408, 414, and 416, slopes towards the connector 407 so that the powder (or liquid) in the compartments, 408 through 418, is directed towards the connector. Each compartments, 408 through 418, has a compartment lid 415 which is fitted to the compartments, 408 through 418, after the compartment has been filled with the respective powder or liquid. In this way, it is not necessary to fill the container, 408 through 418, through the narrow connector 407, which would be difficult. The compartment lids 415 are heat welded (hot melted) to the respective compartments, 408 through 418. As mentioned above, the container lid 403 also forms the lid which closes off the glucose compartment 420 and is heat welded thereto.

[0295] Referring back to Figure 5, a new disposable concentrate container 402 is connected to the manifold 404 at the beginning of a PD treatment session, after disinfection,

and is disconnected and discarded once the treatment has finished. A connection motor 422 engages with the disposable concentrate container 402 and drives the container into connection with the manifold 404.

[0296] Functionally, the compartments, 408 through 420, of the disposable concentrate container 402 are of three types. The first type includes the lactic acid compartment 408, the cleaning agent compartment 410, the calcium chloride compartment 416 and the magnesium chloride compartment 418. This first type of compartment has an air vent channel 424 which extends from an upper region of the interior of the compartment to a direct opening to atmosphere in the manifold 404 when the compartments, 408, 410, 416, and 418, is connected to the manifold 404. The air vent channel 424 allows air to exit the compartments, 408, 410, 416, and 418, when water is introduced into the compartment via a fluid channel 426 of this type of container or when fluid is withdrawn from the compartment, 408, 410, 416, and 418, by means of the fluid channel 426. The fluid channel 426 introduces the fluid in a lower region of the interior of the compartment, 408, 410, 416, and 418, so that the water contacts all of the material as the water level rises up the compartment.

[0297] This first type of compartment, 408, 410, 416, and 418, is used to contain powdered salts which are only required in small amounts, so that the salt can be included in an amount which dissolves completely without additional agitation when a sufficient amount of water is introduced into the compartment, or for salts which are already in a concentrated solution.

[0298] The second type of compartment, 412 and 414, is used for salts which are required in such large volumes that the compartment 412,414 would have to be too large to contain at once all of the water required to dissolve all of the required salt. Thus, compartment 412 contains sodium bicarbonate and compartment 414 contains sodium chloride. This type of compartment includes a combined air vent and fluid channel 428

and a combined priming and output channel 430. Initially the salt in this type of compartment, 412 and 414, is immersed (or primed) by introducing water through the combined priming and output channel 430 in a lower region of the compartment, while air is vented from an upper region of the compartment through the combined air vent and fluid channel 428. The priming operation fills the compartment 412,414 with water to immerse all of the salt therein. A similar technique is described in European Patent No. 278,100, which is incorporated herein by reference.

[0299] Once the salt has been fully wetted, water is drawn through the combined air vent and fluid channel 428 and allowed to percolate through and dissolve the salt, so that salt solution can be drawn off in a lower region of the compartment, 412 and 414, through the combined priming and output channel 430. As the salt solution is drawn from the compartment, 412 and 414, the reduction in pressure causes a corresponding volume of water to enter the compartment, 412 and 414, through the combined air vent and fluid channel 428 which is connected to a source of water.

[0300] It would be possible to operate the second type of compartment, 412 and 414, in a similar manner to the first type of compartment, 408, 410, 416, and 418. For example, the compartment may be filled with water through the output channel 430 to dissolve the salt therein and the (substantially saturated) salt solution may be withdrawn through the output channel 430. Because the amount of salt in the second type of compartment, 412 and 414, is larger than can be dissolved by the volume of water that fills the compartment, 412 and 414, some salt will remain in the compartment, 412 and 414, after the solution is withdrawn. The compartment, 412 and 414, can therefore be refilled with water to obtain more solution.

[0301] The physical configuration of the first and second types of compartment is identical when the container 402 is not connected to the manifold 404. It is only the contents of

the compartment and the arrangement of valves and air vents in the mixing module 400 which determines the type of the compartment.

[0302] The third type of compartment is the glucose compartment 420. Glucose is particularly difficult to dissolve consistently and quickly in high concentrations, such as 50%, and therefore requires recirculation to ensure that all the glucose is dissolved. Furthermore, the volume of the glucose solution decreases as the glucose dissolves and thus the glucose compartment 420 requires continuous venting throughout the dissolution process. Thus, the glucose compartment 420 includes a glucose air vent channel 432 which is permanently connected to atmosphere when the disposable concentrate container 402 is connected to the manifold 404, a fluid input channel 434 which inputs water or recirculated glucose solution to a lower region of the glucose compartment 420, and a glucose output channel 436 which draws glucose solution from an upper region of the glucose compartment 420 through a glucose particle filter 438 which prevents particles of glucose from accidentally entering the fluid system.

[0303] The inventors have found that good results are achieved with monohydrate glucose, specifically LYCADEX PF/Dextrose mono pyrogen free from Roquette Freres S.A. of Lestrem, France, because this glucose is available in the quality required by the European Pharmacopoeia 1997 and is relatively inexpensive. Furthermore, the inventors have found that anhydrous glucose forms a cake when water is added to it which prevents effective dissolution. It is believed that a relatively large particle size is also advantageous in terms of effective dissolution, since large particle size results in improved flowability and less caking.

[0304] Figure 15 shows a sectional view through the lower part of the glucose compartment 420 of the disposable concentrate container 402 in position above the manifold 404, which illustrates the relative positions of the container 402, cap 406 and manifold 404 when the container 402 is loaded into

the apparatus 100. The container 402 is loaded into the apparatus 100 by sliding it horizontally along a pair of container support rails 417. The container support rails 417 engage with projections 419 on the connectors 407 of the container 402 so that the container support rails 417 hold the container 402 in a vertical position. The container support rails 417 are driven by the connection motor 422, see Fig. 5, in the vertical direction to raise or lower the container 402. It should be noted that when the disposable concentrate container 402 is loaded into the apparatus 100, the cap 406 closes off the manifold 404 to prevent outside contamination of the manifold 404 while the interior of the apparatus 100 is necessarily open to the atmosphere. Once the container 402 is loaded into the apparatus 100, the connection motor 422 acts to drive the container 402 downwardly by means of the container support rails 417 onto the cap 406 to keep the cap 406 firmly in position on the manifold 404 during disinfection.

[0305] As shown in Figure 15, the manifold 404 includes a drainage port 441 through which fluid may be drained to a reservoir vent disinfection valve 498, as described below.

[0306] As shown in Figure 15, the connector 407 includes an insert 421 which fits inside the neck of the compartment 420 and retains a septum 423 of silicone rubber or thermoplastic elastomer which seals off the compartment 420 during storage. The insert 421 includes (part of) the projections 419 for engagement with the container support rails 417 and is welded into the neck of the compartment 420. The connectors 407 of each of the compartments, 408 through 420, are all constructed in the same manner.

[0307] Within the compartment 420, a central pipe 425 runs up to the top of the compartment 420, although this is not shown in Figure 15. Each compartment, 408 through 420, has a central pipe 425 which functions as the air vent channel 424, the combined air vent and fluid channel 428, the glucose output channel 436 or the glucose air vent channel 432

depending on the particular compartment, 408 through 420.

[0308] At its upper end (not shown) the central pipe 425 may be received in an annular projection from the compartment lid 415 which is of a larger diameter than the central pipe 425 and circumscribes the central pipe 425. The gap between the annular projection and the wall of the central pipe 425 may act as a filter.

[0309] Alternatively, the central pipe 425 may be provided with an injection moulded filter element 439 as shown in Figure 23.

[0310] Between the base of the central pipe 425 and the sloping floor of the compartment 420, a diffuser 427 is provided in the form of a series of spaced bars extending radially outwardly from the central pipe 425 to the floor of the compartment 420. The diffuser 427 is shown in more detail in Figure 22. The diffuser 427 supports the central pipe 425 in the compartment 420 and also diffuses the flow of water (or other fluid) into the compartment 420 so that the flow is turbulent which agitates the powdered salt (or glucose) in the compartment 420 to aid dissolution. When the turbulent flow of water dissolves the powder in the region of the diffuser 427 the remaining powder falls down inside the compartment 420 so that all of the powder is dissolved.

[0311] In general, each of the compartments, 408 through 420, is constructed in this way. In one possible arrangement (not shown) the glucose compartment 420 has tapered sides extending outwardly in the upward direction which prevent the glucose powder in the compartment from lifting up when water is added. If there is a tendency for the powder to lift, a water channel is formed at the periphery of the compartment. The water dissolves any powder in this region, resulting in that the powder falls down and seals the channel.

[0312] As shown in Figure 15, the manifold 404 comprises a respective spike 429 for each connector 407. The spike 429 is arranged to break through the septum 423 to establish fluid communication between the manifold 404 and the compartment

420. The spike 429 is removably located in the manifold 404 and is intended to be replaced when it has been worn down by successive septa penetrations.

[0313] The spike 429 has a central fluid channel 431 defined therein which connects to the central pipe 425 of the compartment 420 (Figure 17). A further fluid channel 433 is also defined in the spike 429 and, when the container 402 is fitted to the manifold 404, is in fluid communication with the interior of the compartment 420 through the diffuser 427. Thus, the central fluid channel 431 and the central pipe 425 form a combined fluid channel which is concentric with the fluid channel formed by the neck of the connector 407. The type of spike 429 shown in Figure 15 is used to connect to the sodium bicarbonate compartment 412 and the sodium chloride compartment 414 and also the first connector 407a of the glucose compartment 420 to form the fluid input channel 434 and the glucose output channel 436.

[0314] An alternative spike 429a is shown in Figure 18. In this form of spike 429a, the central fluid channel 431a connects the central pipe 425 of the compartment 418 directly to atmosphere so that the central pipe 425 acts as an air vent. This type of spike is used to connect the lactic acid compartment 408, the cleaning agent compartment 410, the calcium chloride compartment 416 and the magnesium chloride compartment 418 to the manifold 404 and also to connect to the second connector 407b of the glucose compartment 420, to form the glucose air vent channel 432.

[0315] As shown in Figure 18, the cap 406 includes a cover portion 435 which fits over the spike 429a when the cap 406 is in position over the manifold 404 for disinfection of the apparatus 100. The cover portion 435 redirects a flow of disinfection fluid which emerges from the further fluid channel 433 back into the central fluid channel 431a, so that the central fluid channel 431a is disinfected. If the cover portion 435 were not present, it would not be possible to direct disinfection fluid through the further fluid channel

433 into the central fluid channel 431a.

[0316] Figure 16 shows the manifold cap 406 removed from the manifold 404. To achieve this from the position shown in Figure 15, the container 402 is lifted by means of the container support rails 417 so that the cap 406 can pivot into the position shown in Figure 16. The cap 406 is attached to the manifold 404 by a spring-biased hinge 437 which ensures that the last part of the cap's movement onto the manifold 404 is linear, rather than rotational, so that there is no lateral abrasion of the seals between the manifold 404 and cap 406. A small D.C. motor (not shown) in the hinge 437 provides the motive power to rotate the cap 406 into and out of position on the manifold 404. Alternatively, a spring mechanism may be used.

[0317] Figure 17 shows the container 402 in position on the manifold 404, with the septum 423 broken by the spike 429.

[0318] Figure 24 and Figure 25 show an alternative design of the compartments, for example compartment 408 or 418. Below, compartment 408 will be described. The design differs from the design described in connection with Figures 13 - 18 mainly in the arrangement of the air vent channel 424 and the fluid channel 426.

[0319] The neck portion of the compartment 408 comprises an insert 542 having a membrane 545 attached to its upper surface. The membrane 545 is for example an aluminium foil, which may be broken and penetrated by a spike 429. The central channel of the spike co-operates with the air vent channel 424 as in the previous designs.

[0320] Integral with the air vent channel 424 is arranged a first tube 544. The first tube may have a circular cross section but any shape is possible. Inside the first tube 544 is arranged a second tube 546 leaving a small space 548 to the first tube 544. At the bottom of first tube 544, the small space 548 opens to the interior of the compartment 408 in a narrow ring-shaped slit 550. The second tube 546 is at the top thereof provided with a hole 552 communicating the interior of

the second tube with the small space 548. At the bottom thereof, the second tube 546 is connected to the ring-shaped channel of the spike 429 as shown.

[0321] In operation, in case of a compartment comprising powder which should be primed, water is entered by means of spike 429 into second tube 546 up to the top thereof. Water passes out through hole 552 to the small space 548 and flows down to the ring-shaped slit 550 from where it is directed sideways along the bottom surface of the compartment to prime and, if applicable, dissolve the powder in the compartment. The small space still maintain most of its air content, since water is passed slowly down along the exterior surface of the second tube 546 and along the interior surface of first tube 544.

[0322] After priming and when fluid is to be taken out from the compartment, a suction is exerted by the spike inside tube 546. Fluid is sucked via slit 550 and upwards in the small space 548 to opening 552. The air in the small slit is moved down the upper portion of the second tube 546 but maintain entrapped there. Fluid fills the rest of the second tube 546. Since the flow is slow in the second tube 546, the air stays in the upper portion.

[0323] If the compartment is disengaged from the spike, the fluid in the second tube 546 is given off to the manifold portion 404 (figure 5). The air cushion in the upper portion of the second tube 546 prevents further fluid to pass upwards in the small space 548, and no further fluid may pass out from the compartment. Thus, drips from the cartridge is prevented, apart from the first few drips at disengagement. In this design, the septum 423 used in the previously described design is no longer necessary.

[0324] Figure 25 shows the same compartment as if figure 24 with the spike in the engaged position.

[0325] This design may be used with the lactic acid compartment 408, which is in liquid form from the start. The same design may also be used for the other compartments

enclosing powder components, inclusive, the glucose compartment.

[0326] Returning to Figure 5, in normal operation of the concentrate mixing module 400, heated purified water from the thermal control and sterilization module 300 enters the concentrate mixing module 400 through the mixing water feed connection 4a. A mixing system bypass valve 440 allows the purified water to be output through the mixing module output connection 4b without being processed by the concentrate mixing module 400, for example for sterilization of downstream components. The water flow into the mixing system may be stopped by a mixing water stop valve 442.

[0327] Downstream of the mixing water stop valve 442 a glucose selector valve 444 is arranged to either allow the purified water to pass or to stop the flow of purified water and pass glucose solution from the glucose compartment 420 to the downstream components of the mixing system. In order to supply water to the glucose compartment 420 for dissolving the glucose, the mixing system bypass valve 440 is opened and a reversible flow control pump 446 is used to draw purified water from the mixing water feed connection 4a and pump it through the glucose selector valve 444 to the glucose compartment 420 via the glucose input valve 490 and fluid input channel 434. The flow control pump 446 is a piston pump of similar construction to the Gambro standard part No. K1 4207 002 but having a 9 mm or 12 mm diameter, rather than the standard 6 mm diameter. A glucose recirculation pump 448, for example a gear pump or a centrifugal pump, recirculates the water through the glucose compartment 420 by means of the fluid input channel 434 and the glucose output channel 436, to ensure total dissolution of the glucose. During recirculation, the glucose input valve 490 is closed and the rest of the mixing module 400 can therefore operate independently while the glucose is being dissolved.

[0328] Downstream of the glucose selector valve 444 a mixing chamber 450 mixes the flow of purified water from the

mixing water feed connection 4a (or glucose solution from the glucose compartment 420) with the flow from a reversible salt input displacement pump 452 (Gambro standard part K1 4207 002).

[0329] The flow control pump 446 is provided with a tachometer 454, and the salt input displacement pump 452 is also provided with a tachometer 456. The tachometers, 454 through 456, monitor the volume flow rates of the respective pumps, 446 through 452, in order to verify correct operation. When a pumping operation is carried out solely under control of the salt input displacement pump 452, the flow control pump 446 is bypassed by opening a flow control pump bypass valve 458. Both the salt input displacement pump 452 and the flow control pump 446 are piston pumps which have the necessary volumetric accuracy to control the salt concentration of the PD fluid. The maximum flow rate through the salt input displacement pump 452 is for example 50 ml/min and the maximum flow rate through the flow control pump 446 is for example 180 ml/min.

[0330] Downstream of the flow control pump 446, two independent mixing conductivity meters 460 monitor the composition of the salt solutions passing there through, in combination with respective independent mixing temperature sensors 462. The two conductivity meters 460 and two temperature sensors 462 are provided for redundancy in the event of the failure of one meter or sensor. One of the meters and one of the temperature sensors communicates with the control system and the other meter and sensor communicate with the protective system, see Fig. 1a.

[0331] Downstream of the mixing conductivity meters 460 and the mixing temperature sensors 462, a drain disinfection valve 464 allows water from the mixing water feed connection 4a to be passed to the mixing module drain connection 15. The drain disinfection valve 464 is activated in this way during disinfection. In this case, the water entering the mixing water feed connection 4a has been heated to disinfection

temperature by the thermal control and sterilization module 300 and is then passed to the drainage module 500 by means of the drain disinfection valve 464 to disinfect the drainage module 500.

[0332] A reservoir filling valve 466 directs the fluid passing through the mixing conductivity meters 460 either to the mixing module output connection 4b or to a concentrate reservoir 468, which is used to store the concentrated PD fluid before it is diluted by a controlled flow of purified water. The concentrate reservoir 468 has a reservoir output valve 470 through which the concentrated PD fluid may be passed to the salt input displacement pump 452.

[0333] The concentrate reservoir 468 also has a reservoir air vent connection 472 which can be opened to atmosphere at the manifold cap 406 under the control of a reservoir air vent valve 496 to vent air during filling or emptying of the concentrate reservoir 468. Because the concentrate reservoir 468 contains concentrated PD fluid which will be supplied to the patient, the reservoir air vent connection 472 is disinfected. In order to achieve this and to disinfect the spikes 429, during disinfection, the manifold cap 406 is lowered onto the manifold 404 to form a sealed cavity as shown in Figure 15. This cavity can be filled with hot disinfecting fluid from the thermal control and sterilization module 300 by means of the mixing water feed connection 4a, as described in detail below. The air which is initially contained within the cavity formed by the manifold 404 and the cap 406 is passed to the drainage module 500 through the mixing module drain connection 15 by means of a cap air vent valve 474. Once all the air has been vented from this cavity, the cap air vent valve 474 provides a connection from the cavity formed by the manifold 404 and the manifold cap 406 to the mixing module drain connection 15 so that disinfection fluid can be circulated through the cavity. In this way, the reservoir air vent connection 472 can be completely disinfected, even though in operation of the system the reservoir air vent connection

472 is open to atmosphere. The reservoir air vent valve 496 is closed during this process, but can be opened once the manifold 404 and manifold cap 406 have been disinfected to pass disinfection fluid from the reservoir air vent connection 472 directly to the mixing module drain connection 15 to disinfect the reservoir air vent valve 496. The cavity formed by the manifold 404 and the manifold cap 406 is drained after disinfection by connecting the cavity to atmosphere at the manifold cap air vent 6 by opening the cap air vent valve 474. Disinfection fluid is then able to drain to the drainage module 500 via the reservoir vent disinfection valve 498, the reservoir air vent valve 496 and the mixing module drain connection 15.

[0334] The dissolution and mixing of the salts from the compartments of the disposable concentrate container 402 is effected by the opening and closing of the valves on the fluid lines, 426 and 430, of the compartments, 408 through 418, such that the salt input displacement pump 452 in a priming step can supply water to, and subsequently withdraw salt solution from, each of the compartments, 408 through 418.

[0335] Each compartment, 408 through 418, of the disposable concentrate container 402 is provided with a respective input valve, namely a lactic acid input valve 478, a cleaning agent input valve 480, a sodium bicarbonate input valve 482, a sodium chloride input valve 484, a calcium chloride input valve 486 and a magnesium chloride input valve 488. In addition, the function of the combined air vent and fluid channels 428 of the sodium bicarbonate compartment 412 and the sodium chloride compartment 414 is controlled by a sodium bicarbonate air vent valve 492 and a sodium chloride air vent valve 494, respectively.

[0336] The correct operation of these valves, 478 through 488, is monitored using a salt input pressure sensor 476 in the following manner. After one of the input valves, 478 through 488, has been operated and is closed, a signal is sent to all of the input valves, 478 through 488, to close the

valves. The salt input displacement pump 452 is then energised to pump water from the mixing water feed connection 4a towards the input valves, 478 through 488. The pressure generated by the salt input displacement pump 452 is monitored by the salt input pressure sensor 476. In the event that one of the input valves, 478 through 488, is stuck in the open position, a sufficiently high pressure will not be attainable and this fault condition will be detected by the salt input pressure sensor 476.

[0337] In the case of the first type of compartment, 408, 410, 416, and 418, described above and taking the calcium chloride compartment 416 as an example, water from the mixing water feed connection 4a is drawn by the salt input displacement pump 452 through the mixing chamber 450 and is pumped through the calcium chloride input valve 486 into the calcium chloride compartment 416 via the fluid channel 426 of that compartment. All other input valves, 478 through 488, of the other compartments, 408 through 418, are closed. The air in the calcium chloride compartment 416 which is displaced by the water pumped into that compartment is vented to atmosphere through the air vent channel 424.

[0338] When the salt input displacement pump 452 has passed the required amount of water into the calcium chloride compartment 416, it is expected that all the calcium chloride powder that was in the compartment when the disposable concentrate container was loaded has been dissolved. The weight of calcium chloride in the calcium chloride compartment 416 is predetermined and the volume of water passed by the salt input displacement pump 452 is known, such that an approximation of the concentration of the calcium chloride solution formed in the calcium chloride compartment 416 can be derived.

[0339] The displacement pump 452 is driven by a step motor. Each step corresponds to a well defined volume of fluid pumped, dependent on the rotational position of the step motor. The control system of the pump motor calculates the

volume pumped by the pump in a accurate manner.

[0340] In order to transfer the necessary amount of calcium chloride solution to the concentrate reservoir 468, the flow control pump 446 is activated to draw water from the mixing water feed connection 4a at a predefined rate. The water is directed to the mixing module drain connection 15 by the drain disinfection valve 464. The salt input displacement pump 452 is activated to pump the calcium chloride solution at a controlled volume flow rate through the mixing chamber 450 via the flow control pump 446 through the mixing conductivity meters 460 to the mixing module drain connection 15. The flow rate through the mixing water feed connection 4a is reduced by an amount equal to the flow rate generated by the salt input displacement pump 452 because the flow rate through the flow control pump 446 is constant, whereby a predetermined dilution ratio is obtained. The mixing conductivity meters 460 measures the conductivity, and thus the concentration, of the diluted calcium chloride solution and the flow rate of the salt input displacement pump 452 is adjusted to achieve a predetermined concentration. Once the concentration is achieved, the drain disinfection valve 464 is switched and the reservoir filling valve 466 directs the calcium chloride solution to the concentrate reservoir 468, where it is stored until all the components of the concentrated PD fluid have been prepared. The total volume and the concentration of the calcium chloride solution which has passed through the flow control pump 446 into the concentrate reservoir 468 is therefore known and thus the amount of calcium chloride present in the concentrate reservoir. It is noted that the order of introduction of salts is closer described below.

[0341] A similar process to that for the dissolution and measurement of the calcium chloride solution is used for the preparation of the magnesium chloride solution from the magnesium chloride compartment 418. The cleaning agent is also dissolved in the cleaning agent compartment 410 in this way, when required. The lactic acid is routed to the concentrate

reservoir 468 without dilution. As explained below, the solution created with the cleaning agent is not a component of the PD fluid.

[0342] The solutions of sodium bicarbonate and sodium chloride are produced in a different manner to those for magnesium chloride and calcium chloride, because sodium bicarbonate and sodium chloride are used in greater amounts than magnesium chloride and calcium chloride. Taking as an example the preparation of sodium bicarbonate, all of the input valves, 478 through 488, are closed, except for the sodium bicarbonate input valve 482. The sodium bicarbonate air vent valve 492 is set such that the combined air vent and fluid channel 428 of the sodium bicarbonate compartment 412 is connected to atmosphere by means of the manifold 404. The salt input displacement pump 452 pumps a measured quantity of water from the mixing water feed connection 4a by means of the mixing chamber 450 through the sodium bicarbonate input valve 482 and into the sodium bicarbonate compartment 412 by means of the combined priming and output channel 430. Sufficient water is introduced into the sodium bicarbonate compartment 412 that the sodium bicarbonate powder in the compartment 412 is fully immersed in water.

[0343] Once the sodium bicarbonate powder in the sodium bicarbonate compartment 412 is fully immersed the sodium bicarbonate air vent valve 492 is switched to provide a fluid path from the mixing water feed connection 4a to the combined air vent and fluid channel 428 of the sodium bicarbonate compartment 412. The salt input displacement pump 452 is reversed and draws a substantially saturated sodium bicarbonate solution out of the sodium bicarbonate compartment 412 through the combined priming and output channel 430 and the sodium bicarbonate input valve 482. The conductivity of the sodium bicarbonate solution is controlled and the solution is diluted and stored in the concentrate reservoir 468 in the same manner as for the calcium chloride solution described above.

[0344] The mixing and measuring of the sodium chloride solution is carried out in a corresponding manner.

[0345] The amounts of salt in each of the compartments, 408 through 418, are chosen such that in correct operation each compartment, 408 through 418, produces a salt solution with a characteristic conductivity. Thus, if a malfunction of the system occurs whereby the wrong salt solution, for example magnesium chloride instead of calcium chloride, is produced, this will be identifiable from the conductivity measurement.

[0346] Furthermore, the salts are mixed at relatively high concentrations which provides an environment in which bacteria are unable to survive and thereby aids bacteriological control. The relatively high concentrations also allow the conductivity meters 460 to operate in a range in which measurement errors are relatively insignificant compared to the measured values, thereby increasing the accuracy of the concentration measurements.

[0347] The dissolution of the glucose solution has been described above. A required amount of the glucose solution is pumped to the concentrate reservoir 468 by means of the glucose input valve 490, glucose selector valve 444 and the reservoir filling valve 466 by the flow control pump 446. This pump is used because it has a high capacity, whereby the metering of the glucose may take place in a shorter time.

[0348] At the end of the dissolution and measuring operation, the concentrate reservoir 468 contains concentrated PD fluid with the correct relative proportions of salts and glucose required by the patient's individual prescription but at a higher absolute concentration. Thus, it is then only necessary to add water to this concentrated PD fluid to obtain PD fluid according to the patient's prescription.

[0349] When it is desired to provide the PD fluid to the patient through the mixing module output connection 4b, a measured flow (around 50 ml/min) of concentrated PD fluid is drawn from the concentrate reservoir 468 by means of the reservoir output valve 470 by the salt input displacement pump

452, which pumps the concentrated PD fluid into the mixing chamber 450. The flow control pump 446 is bypassed by opening a flow control pump bypass valve 458 and a constant flow (around 300 ml/min) of PD fluid is drawn out of the mixing module output connection 4b by the volumetric pump 352 of the thermal control and sterilization module 300, see figure 4. The flow out of the mixing module output connection 4b is greater than that produced by the salt input displacement pump 452, and the additional fluid flow (around 250 ml/min) that is not provided by the salt input displacement pump 452 is drawn from the mixing water feed connection 4a. In this way, the concentrated PD fluid from the concentrate reservoir 468 is diluted in the mixing chamber 450 with water from the mixing water feed connection 4a so that PD fluid at the desired concentration exits the concentrate mixing module 400 via the mixing module output connection 4b. The concentration of the PD fluid is monitored by the mixing conductivity meters 460 and is controlled by varying the flow rate through the salt input displacement pump 452.

[0350] The dilution of the concentrated PD fluid from the concentrate reservoir 468 in this way not only reduces the salt and glucose concentration of the PD fluid to the required level, but also ensures that the level of dissolved gas in the PD fluid is low and below the medically required maximum level. The inventors have assumed that by the time the concentrated PD fluid in the concentrate reservoir 468 is ready for use it will be, at most, saturated with dissolved gas which has entered the system during dissolution of the salts and glucose. However, the water entering the concentrate mixing module 400 at the mixing water feed connection 4a has been degassed by the water preparation module 200. The dilution ratio of the flows of the concentrated dialysis fluid pumped by the salt input displacement pump 452 and the water entering the mixing water feed connection 4a has been chosen to be at least sufficient to dilute the gas-saturated concentrated dialysis fluid to a dissolved gas content below

the medically required level.

[0351] The flow through the RO membrane disinfection connection 3 is controlled by an RO membrane disinfection valve 499. During disinfection, water at disinfection temperature is supplied to the mixing water feed connection 4a by the thermal control and sterilization module 300 and is pumped by the salt input displacement pump 452 through the mixing water stop valve 442, the glucose selector valve 444, the mixing chamber 450 and the RO membrane disinfection valve 499 via the RO membrane disinfection connection 3 to the water preparation module 200.

[0352] After the concentrate disposable container 402 is put in place and into engagement with the spikes 429 in the manifold 404, the following sequence of operations takes place.

[0353] First, the cleaning agent compartment 410 is primed with water by the introduction of 80 ml of water into the cleaning agent compartment 410, which comprises 20 g sodium carbonate, in order to thereby produce a sodium carbonate solution having a concentration of about 2284 mmol/l. The sodium carbonate solution is used for cleaning purpose as described above.

[0354] The peritoneal dialysis fluid is composed from six separate substances namely magnesium chloride, calcium chloride, sodium bicarbonate, sodium chloride, lactic acid and glucose. The amount of material in each compartment, 410 through 420, is given in Table 2.

[0355] In order to prime the disposable concentrate container 402, firstly 962 ml of water is introduced into the glucose compartment 420 by the flow control pump 446. Since the flow control pump 446 can operate at about 180 ml/min, this introduction will take approximately 5.5 minutes. Then the glucose input valve 490 is closed and the glucose recirculation pump 448 is operated in order to recirculate the glucose in the glucose compartment 420 to promote full dissolution.

[0356] Thereafter, the magnesium chloride input valve 488 is opened to introduce 48.4 ml of water into the magnesium chloride compartment 418. Then the magnesium chloride input valve 488 is closed and the calcium chloride input valve 486 is opened to introduce 145.2 ml of water into the calcium chloride compartment 416. These introductions of water are performed by the salt input displacement pump 452, which has a maximum capacity of about 50 ml/min. The above two priming steps will take about 4 minutes together. The magnesium chloride and the calcium chloride are fully dissolved in the water introduced, either during the introduction of water into the compartment or shortly thereafter to finally dissolve all of the salt particles.

[0357] Then the water is introduced into the sodium bicarbonate compartment 412 by opening the sodium bicarbonate input valve 482 and introducing about 60 ml of water by means of the salt input displacement pump 452. The exact amount of water introduced into the sodium bicarbonate compartment 412 is not crucial provided the water level does not rise above the combined air vent and fluid channel 428 so that water is not passed down that channel 428 to the manifold 404 by means of the sodium bicarbonate air vent valve 492. If a small portion of the water nevertheless does pass this way, this is of no consequence.

[0358] The same procedure is performed for the sodium chloride compartment 414 by the introduction of approximately 100 ml of water into the compartment by means of the salt input displacement pump 452. All of the powder in the sodium bicarbonate compartment 412 and the sodium chloride compartment 414 is not completely dissolved, because the water quantity is insufficient to dissolve all of the powder.

[0359] No water is added to the lactic acid compartment 408, which comprises 120 g lactic acid having a concentration of 30%.

[0360] By means of the above described priming procedure, the different compartments, 408 through 420, will comprise

electrolyte solutions of the salts and glucose having the following concentrations when taken out from the respective compartments at 25°C:

magnesium chloride	2455.8 mmol/l
calcium chloride	2117.3 mmol/l
sodium bicarbonate	1199 mmol/l
sodium chloride	5253 mmol/l
lactic acid	3500 mmol/l
Glucose	3393.6 mmol/l

[0361] The exact order of priming of the compartments may differ from the order given above.

[0362] The next step in the procedure is to transfer measured amounts of the electrolytes and the glucose to the concentrate reservoir 468. The resulting solution in the concentrate reservoir 468 may be a solution having five times the concentration of the final required solution. The concentrate reservoir solution is then diluted by 1:5 before being sent to the OLA 375 for sterilization before introduction into the peritoneal cavity of the patient. Thus, the concentrate reservoir 468 should comprise 600 ml of concentrated solution in order to provide 3000 ml of final peritoneal dialysis solution after dilution.

[0363] The first substance to be introduced into the concentrate reservoir 468 is sodium bicarbonate. The sodium bicarbonate air vent valve 492 is adjusted to connect the combined air vent and fluid channel 428 with the mixing water feed connection 4a and the sodium bicarbonate input valve 482 is opened to connect the combined priming and output channel 430 with the salt input displacement pump 452. By operating the salt input displacement pump 452, substantially saturated sodium bicarbonate solution is taken out from the bottom of the sodium bicarbonate compartment 412 and water from the water preparation module 200 is introduced into the top of the sodium bicarbonate compartment 412 via the combined air vent and fluid channel 428. In order to provide a bicarbonate concentration of 40 mmol/l in the final solution, it is

required to transfer 120 mmol of sodium bicarbonate to the concentrate reservoir 468, which corresponds to 100 ml pumped by the salt input displacement pump 452. Thus, the salt input displacement pump 452 may be operated at a pump speed of 40 ml/min in 2.5 minutes in order to provide the required amount. At the same time the flow control pump 446 is adjusted to 60 ml/min in order to obtain a dilution ratio of 1:1.5 resulting in a conductivity of approximately 35 mS/cm.

[0364] As described before, the mixed solution is passed to the drainage module 500 by means of the drain disinfection valve 464 and the mixing module drain connection 15 until a stable value has been obtained from the mixing conductivity meters 460. Then the drain disinfection valve 464 and the reservoir filling valve 466 are switched over in order to transfer the solution to the concentrate reservoir 466.

[0365] The conductivity measurement at the mixing conductivity meters 460 is converted to the corresponding concentration of sodium bicarbonate by the control system and is multiplied by the flow velocity as measured by tachometer 454 of the flow control pump 446 to thereby obtain the amount of sodium bicarbonate per minute passing through the mixing conductivity meters 460. By integrating this amount per minute over time, the total amount of material delivered to the concentrate reservoir 468 is obtained. When 120 mmol have been transferred, the reservoir filling valve 464 is switched over in order to stop further introduction into the concentrate reservoir 468 and direct the solution to the drainage module 500 by means of the mixing module drain connection 15. The fact that the correct amount of material has been delivered to the concentrate reservoir 468 can also be controlled by the tachometer 456 of the salt input displacement pump 452, which should pump 100 ml.

[0366] Immediately after the shifting over of the reservoir filling valve 464, the salt input displacement pump 452 is reversed to pump clean water in the opposite direction to push back the sodium bicarbonate present in the tubes between the

sodium bicarbonate input valve 482 and the mixing chamber 450, in order to save material and also in order to flush the tube system with clean water. The volume of substantially saturated sodium bicarbonate so recovered is relative small, but may still be significant. A corresponding volume of air is transferred into combined air vent and fluid channel 428 since there is normally an air cushion at the top of compartment 412. During the next operation of the compartment, this air volume is reintroduced into compartment 412.

[0367] The flow control pump 446 operates to flush the rest of the pipe system downstream of the mixing chamber 450 of any sodium bicarbonate.

[0368] If the peritoneal dialysis fluid is to comprise substantially only bicarbonate as buffer, the final concentration of the buffer can be adjusted by the adjustment of the amount of bicarbonate introduced into the concentrate reservoir 468. Introduction of 100 ml will result in a final bicarbonate concentration of 40 mmol/l and introduction of 87.5 ml will result in a final bicarbonate concentration of 35 mmol/l. The pH may be adjusted by the addition of lactic acid.

[0369] If the final peritoneal dialysis fluid is to comprise a mixture of sodium bicarbonate and sodium lactate, for example 25 mmol/l bicarbonate and 15 mmol/l sodium lactate, the following procedure is followed. Any mixture from about 5:35 to 35:5 can be obtained or any other total sum than 40.

[0370] The lactic acid input valve 478 is opened to connect the lactic acid compartment 408 with the salt input displacement pump 452. The mixing water stop valve 442 is closed to prevent dilution of the lactic acid and the flow control pump bypass valve 458 is opened to bypass the flow control pump 446. If 15 mmol/l of sodium lactate is desired, the salt input displacement pump 452 pumps 16 ml of lactic acid (30% concentration) into the concentrate reservoir 468. The concentration of the lactic acid solution may be monitored by the mixing conductivity meters 460, which should show a

conductivity value of approximately 39 mS/cm.

[0371] During the introduction of lactic acid into the bicarbonate solution in the concentrate reservoir 468, the acid reacts with the bicarbonate ions and forms carbon dioxide, which is vented to atmosphere via the reservoir air vent connection 472, the reservoir air vent valve 496 and the cap air vent valve 474. At the top of the concentrate reservoir 468, a cushion of carbon dioxide is formed, which is not transferred to the surrounding atmosphere. Thus, the carbon dioxide partial pressure will be one atmosphere (1 Bar) which results in a dissolved carbon dioxide concentration of about 23 mmol/l at equilibrium in the liquid in the concentrate reservoir. The formation of carbon dioxide is comparatively fast, but a short pause may be required until the carbon dioxide generation has ceased.

[0372] Once again the salt input displacement pump 452 is reversed for pushing back the lactic acid into the lactic acid compartment 408 until water reaches the lactic acid input valve 478 or shortly there before, and the tube system is flushed with water by means of the flow control pump 446.

[0373] Next, sodium chloride is introduced into the concentrate reservoir 468. In order to provide 140 mmol/l in the final solution, 470 mmol has to be transferred to the concentrate reservoir 468, which corresponds to 80 ml of concentrated solution. Since sodium chloride has a very high conductivity, the sodium chloride is diluted as much as possible in the mixing chamber 450. However, the dilution can not be too large because of restrictions in the final volume in the concentrate reservoir 468. As an example a dilution ratio of 1:4 is given below. Thus, the flow control pump 446 is adjusted to 40 ml/minute and the salt input displacement pump 452 is adjusted to 160 ml/min resulting in a conductivity of about 98 mS/cm. The same integration method as described above for sodium bicarbonate is used in order to determine when a sufficient amount of sodium chloride has been introduced into the concentrate reservoir 468. Alternatively,

it is determined when the salt input displacement pump 452 has pumped 80 ml, which should be approximately after two minutes.

[0374] Again the salt input displacement pump 452 is reversed to push back the sodium chloride solution into the sodium chloride compartment 414 and some air into combined air vent and fluid channel 428.

[0375] Then, the glucose input valve 490 is opened to transfer glucose to the concentrate reservoir 468. If 1.5% final glucose concentration is to be obtained, 75 ml glucose solution should be transferred, if 2.5% is to be obtained, 125 ml should be transferred, and if 4.0% is to be obtained, 200 ml should be transferred. In order to save time, the flow control pump 446 is used for this purpose. Glucose has no inherent conductivity, which is checked by the mixing conductivity meters 460. When the correct amount has been introduced as measured by tachometer 454, the glucose selector valve 444 is operated to transfer water from the mixing water feed connection 4a via the flow control pump 446 to flush the tube system. The flow control pump 446 may first be reversed while the mixing system bypass valve 440 is opened to push back glucose to the glucose compartment 420 as described above, if desired. Since the recovered volume is small compared to the volume in the glucose department, the recovery may not be used for glucose.

[0376] The dilution ratio of sodium chloride is selected in dependence on the desired glucose concentration so that the volume obtained in the concentrate reservoir 468 so far is approximately 570 ml.

[0377] Finally, magnesium and calcium are introduced into the concentrate reservoir 468. These substances are introduced as late as possible when the bicarbonate is diluted to a low concentration to avoid problems with precipitation.

[0378] First magnesium chloride is introduced by opening the magnesium chloride input valve 488 and operating the salt input displacement pump 452. Only 1.5 mmol magnesium chloride should be transferred by the salt input displacement pump 452,

which corresponds to 0.6 ml, to obtain a final concentration of 0.5 mmol/l. The salt input displacement pump 452 is able to meter such small quantities with sufficient accuracy. The pump has a displacement of 228 microliter per revolution and is controlled over 1/100 revolution.

[0379] Magnesium chloride is not introduced in concentrated form into the concentrate reservoir 468 to avoid local precipitation. Thus, the flow control pump 446 is operated with 10 times the speed of the salt input displacement pump 452 to obtain a dilution ratio of 1:10. Then the conductivity of the magnesium chloride solution will be around 35 mS/cm. By integrating the concentration obtained from the mixing conductivity meters 460 multiplied with the flow velocity obtained from the flow control pump 446, the delivered amount is obtained. The delivered amount is checked by the salt input displacement pump 452, which should pump 0.6 ml. After completion of the introduction into the concentrate reservoir 468, the salt input displacement pump 452 is reversed to push back magnesium chloride into the magnesium chloride compartment 418. This procedure is of importance for magnesium chloride and calcium chloride, which are provided in small quantities.

[0380] Finally, the same procedure is performed for calcium chloride. In order to provide 1.5 mmol/l calcium in the final solution, it is necessary to transfer 4.5 mmol corresponding to 2.1 ml concentrated solution to the concentrate reservoir 468. As for magnesium, this process is performed by dilution in the ratio of 1:10. The conductivity will then be approximately 34 mS/cm.

[0381] When calcium ions are mixed with bicarbonate ions, there is always a risk of calcium carbonate precipitation. By keeping an air cushion comprising carbon dioxide above the surface of the concentrate reservoir 468 and thereby providing a saturated carbon dioxide gas content in the solution, it is assured that the pH of the solution is as low as possible, whereby no precipitation will take place.

[0382] To assure the highest possible content of carbon dioxide before mixture with calcium chloride, lactic acid may be introduced as late as possible in the mixing procedure, i.e. immediately before the addition of magnesium chloride and calcium chloride, to obtain carbon dioxide generation and saturation of the complete solution with carbon dioxide. The order of sodium bicarbonate, sodium chloride and glucose may also be different from that given above, for example first sodium chloride, then glucose and then sodium bicarbonate.

[0383] After the formation of the concentrated PD solution in the concentrate reservoir 468, it is diluted in the ratio of 1:5. In this mode of operation, the OLA pump 352 is operated at 300 ml/min and the salt input displacement pump 452 is operated at 60 ml/min to obtain a dilution ratio of 1:5. The mixing conductivity meters 460 control the concentration of the mixed solution and adjust the salt input displacement pump 452 to avoid variation in the conductivity.

[0384] A slightly modified mixing portion is disclosed in Figure 5a. A metering pump 448a is inserted in the pipe between the glucose input valve 490 and the glucose selector valve 444. The metering pump 446a is shunted by a valve 490a. The glucose selector valve 444 is replaced by a direct connection to the mixing chamber 450. These additional components enable the measurement of the glucose concentration in the glucose compartment 420. The operation is as follows.

[0385] After dissolution of the glucose in the water introduced into the glucose compartment 420, the glucose should have a concentration of 50%. However, there is always a risk of errors and there is a desire to be able to control the glucose concentration.

[0386] To start this glucose check procedure, the sodium chloride input valve 484 and the sodium chloride air vent valve 494 are opened, the salt input displacement pump 452 is operated and the flow control pump 446 is operated in order to provide a sodium chloride solution having a concentration of about 500 mmol/l, i.e. a dissolution ratio of about 1:10. The

mixing conductivity meters 460 should measure approximately 46.7 mS/cm. The flow control pump 446 is operated at approximately 50 ml/min and the salt input displacement pump 452 at approximately 5 ml/min. Then the glucose input valve 490 is opened and the metering pump 448a is operated to pump glucose solution from the glucose compartment 420 via the fluid input channel 434, the glucose input valve 490 and the metering pump 448a into the mixing chamber 450. The metering pump 448a is driven at for example 20 ml/min.

[0387] The introduction of glucose into the sodium chloride solution in the mixing chamber 450 results in a decrease of the conductivity as measured by the mixing conductivity meters 460. The decrease is substantially proportional to the concentration of the glucose solution. Thus, the glucose concentration in the glucose compartment 420 can be monitored.

[0388] After measuring the glucose concentration, the above described procedure may take place.

[0389] Alternatively, the mixture obtained as described in relation to Figure 5a, i.e. a mixture of glucose and sodium chloride, may be transferred to the concentrate reservoir 468. In that case, the sodium salt input displacement 452 should have a higher speed to ensure that the amount of water introduced into the concentrate reservoir 468 is not too high.

[0390] It is possible to obtain the same operation by using the glucose recirculation pump 448 as a reversible metering pump instead of a separate metering pump 448a.

[0391] It would also be possible to use the lactic acid and dilute it with glucose to monitor the lowering of conductivity. In that case, no additional pump is required compared to Fig. 5. The operation would be to open the lactic acid input valve 478, adjust the salt input displacement pump 452 to 10 ml/min, adjust the flow control pump 446 to 15 ml/min, with the glucose selector valve 444 and the mixing water stop valve 442 open to permit 5 ml/min of water to pass into the mixing chamber 450 from the mixing water feed connection 4a. The conductivity is measured. Then, the glucose

input valve 490 is opened and the glucose selector valve 444 is switched over to replace the water supply (5 ml/min) to the mixing chamber 450 with glucose. The decrease in conductivity is monitored and a calculation is made to determine the corresponding concentration of glucose.

[0392] In Figure 5a there is shown an electric heater 438a in the fluid input channel 434 to glucose compartment 420 to heat the recirculated glucose solution during the dissolution process to promote dissolution. Glucose becomes cooler during dissolution and therefor needs heating to maintain a temperature of for example 40°C during the complete dissolution step.

[0393] Another alternative design of the glucose metering step is shown on Fig. 5b and Fig 4a. Turning first to Fig. 5b, the metering pump 448a has been replaced by a reversible metering pump 448b. Metering pump 448b is constructed to be able to pump the glucose solution against a back pressure of several bar, more than 3 bar and preferably more than 6 bar or reasons appearing below. A valve 490a bypasses the pump 448b. A glucose input valve 490b is arranged between mixing chamber 450 and inlet tube 434 to prime the glucose in compartment 420.

[0394] The operation of the alternative arrangement according to Fig. 5b is the same as described above in connection with Fig. 5 or Fig. 5a, except that the glucose is not entered in concentrate reservoir 468. Instead, the concentrated glucose is metered by metering pump 448b and transferred via the activated valve 490b to an outlet connection 4c, leading to an input connection in the middle of the OLA sterilizer, as indicated on Fig. 4a.

[0395] In the alternative OLA sterilizer arrangement shown of Fig. 4a, the oil bath arrangement 364 - 368 is replaced by an electric heater 364a. The inlet fluid entering the OLA arrangement via inlet 4b, valve 356 and heat exchangers 360 and 362 is an electrolyte fluid having components which are not sensitive to heat. Thus, the electrolyte fluid may be

heated with an electric heater without risk of decomposition or the formation of harmful substances, although an electric heater may have spots of high temperature. The heat sensitive portion of the final solution, namely the glucose is entered after the electric heater 364a at inlet 4c. At this position, the electrolyte fluid is at a high temperature of for example 150°C and at a high pressure of for example 6 bar absolute pressure. The inlet fluid heats the concentrated glucose solution rapidly to a high temperature of for example 148°C. The combined fluid is maintained at a high temperature for a predetermined time period determined by the flow distance in a coil 363. Then, the combined fluid is cooled rapidly in heat exchangers 362 and 360. The temperature is monitored by temperature sensors 370. By this operation, the sensitive glucose portion is heated in a substantially square temperature curve, which is beneficial for the sterilization and for avoiding the formation of glucose degradation products. The sterilization of the glucose portion may be very well controlled in order not to over-sterilize the glucose. The fact that the electrolyte fluid may become slightly over-sterilized means no disadvantage.

[0396] It is possible to include calcium and magnesium ions in the glucose fluid to be late introduced in the OLA arrangement of Fig. 4a in order to avoid possible problems with calcium carbonate precipitation and scaling of the tube portions in the mixing arrangement of Fig. 5b. In this embodiment, calcium chloride and magnesium chloride is transferred to the glucose compartment 420 after the dissolution of the glucose but before the metering of the glucose to output connection 4b. Valve 486 is opened and pump 452 is operated to withdraw calcium chloride from compartment 424. Valve 442 and valve 458 are closed and pump 446 is inoperative. Valve 490 b is placed in the position shown on Fig. 5b and valve 490a is opened. The calcium chloride fluid metered by pump 452 must pass via mixing chamber 450 and valves 490b and 490a to the glucose compartment 420. The

amount of calcium chloride transferred to glucose compartment 420 is carefully monitored by the metering pump 452. The same operation takes place for magnesium chloride.

[0397] Finally, the combined glucose, calcium chloride and magnesium chloride is metered to output 4c to be included in the final PD fluid. By this arrangement, sodium bicarbonate and calcium chloride are not mixed until in the diluted PD fluid, which means that the risk of precipitation is minimised.

[0398] Alternatively, the calcium chloride may be metered by metering pump 452 to mixing chamber 450. Flow control pump 446 is operated to dilute the calcium chloride and the fluid is measured in conductivity meters 460. The measured and diluted calcium chloride is then transferred to glucose chamber via a valve 464a shown in broken lines in Fig. 5b. The same operation takes place with magnesium chloride.

[0399] Alternatively, or in combination, (part of) calcium chloride and/or magnesium chloride may be transferred to concentrate reservoir 468 as previously described.

[0400] Drainage Module 500

[0401] The drainage module 500 is shown in detail in Figure 6. The fluid supplied to the drainage module 500 by the ambient pressure drain connection 14b and the mixing module drain connection 15 is routed directly to the heat recovery drain connection 13b from which it passes to the thermal control and sterilization module 300 for heat recovery before being returned to the heat recovery drain return connection 13c. The fluid entering the heat recovery drain return connection 13c passes to the external waste connection 16 by means of a heat recovery return valve 532. The temperature of the fluid exiting the heat recovery drain connection 13b is monitored by a drain disinfection temperature sensor 530.

[0402] Water from the thermal drain connection 13a, which originates from the purification waste connection 2d of the water preparation module 200, passes through a thermal drain connection valve 520 directly to the external drain connection

16.

[0403] Fluid from the negative pressure drain connection 14a passes through a pressure conditioning chamber 510 under a negative pressure generated by a drainage pump 508 and then passes to the heat recovery drain connection 13b by means of the drain disinfection temperature sensor 530. The pressure conditioning chamber 510 is in the form of a chamber closed by a movable, spring-biased diaphragm, and is provided to prevent pressure fluctuations due to the drainage pump 508 from being passed to the patient along the negative pressure drain connection 14a, and also to make control of the draining process easier. The drainage pump may be a peristaltic pump or gear pump, or a pump generating a predetermined maximum pressure, like a centrifugal pump.

[0404] The conditioning chamber 510 moreover ensures that the patient is not exposed to large negative pressures. For this purpose, the conditioning chamber 510 may be provided with limit switches 512 and 514 that monitors the position of a spring loaded piston 516 in the chamber 510. The switches may be used for controlling the drainage pump 508 to provide a negative pressure compatible with safe patient conditions during drainage of the patient, such as not exceeding 1 meter of water pillar negative pressure in relation to the atmosphere.

[0405] For disinfection, hot disinfecting fluid enters the drainage module 500 through the mixing module drain connection 15, the negative pressure drain connection 14a and the ambient pressure drain connection 14b. The disinfecting fluid is passed from the drainage module 500 along the heat recovery drain connection 13b to the thermal control and sterilization module 300 by means of the drain disinfection temperature sensor 530. The heat from the disinfection fluid is recovered in the thermal control and sterilization module 300 and the fluid is returned to the drainage module 500 by means of the heat recovery drain return connection 13c which passes the fluid to the external waste connection 16 by means of the heat

recovery return valve 532. Chemical disinfectant (or hot water in the case of heat disinfection) from the water preparation module 200 enters the drainage module 500 through the thermal drain connection 13a and passes directly to the external drain connection 16.

[0406] Cyclor and sterilizable connector module 600

[0407] The cyclor and sterilizable connector module 600 is shown in detail in Figure 7. In normal operation, sterile PD fluid is provided to the cyclor and sterilizable connector module 600 by means of the sterile fluid connection 8a and passes through a patient fill valve 602 to a dialysate line sterilizable connector 604. The sterilizable connector 604 may be of the type described in International patent application WO96/05883 (Gambro AB) which is incorporated herein by reference.

[0408] The operation of the sterilizable connector 604 is shown schematically in Figures 19a to 19d. Referring to Figure 19a, the sterilizable connector 604 is arranged to receive a double male connector 630 at the end of the disposable fluid line 10 in two corresponding chambers 632. The end of each prong of the male connector 630 is closed by a pierceable membrane 634. The membranes 634 are pierced by respective membrane spikes 636 when the male connector 630 is fully inserted in the chambers 632, as shown in Figure 19c. The membrane spikes 636 have channels defined there through for fluid flow in the direction of the arrows in Figures 19b and 19c. The chambers 632 are connected by a fluid passage 638 which can be opened or closed by a connector valve 640. In an alternative embodiment, there is no connector valve 640, as shown in Fig. 19b.

[0409] Initially, the male connector 630 is partially inserted into the chambers 632 as shown in Figure 19b. The connector valve 640 is opened and water at sterilization temperature and pressure (3 bar) is circulated through the membrane spikes 636, the chambers 632 and the fluid passage 638 in the direction of the arrows in Figure 19b. The

circulation of the sterilizing water sterilizes the chambers 632, the membranes 634 and the membrane spikes 636. Once this sterilization operation has been completed, the male connector 630 is inserted all the way into the chambers 632, so that the membranes 634 are pierced and a fluid path is opened through the membrane spikes and into the disposable dialysate line 10. At the same time, the fluid connection between the chamber 632 and the fluid passage 638, as well as an area around the spikes, is closed off by the male connector 630. Fluid, for example PD fluid, can then flow in the direction of the arrows shown in Figure 19c during a rinsing step or for filling and draining a peritoneal cavity of a patient.

[0410] At the end of the treatment session, the flow of PD fluid into the sterilizable connector 604 is stopped, the connector valve 640 is closed and the male connector 630 is partially withdrawn from the chambers 632 so that air can enter the disposable fluid line 10 through a recess 642 formed in the wall of the inlet chambers 632. The remaining fluid in the disposable fluid line 10 can then be pumped out to drain the disposable dialysate line 10, as indicated by the arrows in Figure 19d.

[0411] Referring back to Figure 7, from the sterilizable connector 604, the PD fluid passes out of the patient fill connection 9a through the disposable fluid line 10 to the patient's peritoneal cavity. Patient pinch valves 624, which open and close together, are provided on the patient fill connection 9a and the patient drain connection 9b to allow the machine to physically stop the flow of PD fluid in an emergency by pinching the disposable fluid line 10 between two jaws (not shown) which are normally closed. The pinch valves 624 are only opened by the control system and the protective system if it is sure that the apparatus is operating correctly and it is safe to deliver PD fluid to the patient.

[0412] The pinch valves are also opened during insertion of the disposable line set before use.

[0413] Figure 20 shows the disposable fluid line 10 for

connection to the sterilizable connector 604. From the male connector 630, two separate tubes 644 extend to a Y-connector 646. The Y-connector 646 connects the two pipes 644 to a standard catheter connector 654 via a manual pinch valve 648. The catheter connector 654 is the only patient connection in the whole apparatus 100 which is not machine sterilized. In contrast, traditional PD treatment systems include several aseptic connections which may introduce potentially harmful bacteria into the peritoneal cavity and lead to peritonitis. Because the apparatus includes only one aseptic connection, the risk of peritonitis is significantly reduced. The only aseptic connection may be replaced by a sterile connection, for example a connection performed by a sterile welding device, cutting a portion of the end of the line set 10 and a portion of a patient tube with a hot wafer and immediately joining the hot ends to obtain a sterile connection. The patient tube is partially consumed and need to be replaced with certain intervals. This technique is well known and used. Another connection technique claimed to be sterile is a connector sterilized by ultraviolet light during the connection cycle.

[0414] The distance between the Y-connector 646 and the catheter connector 654 is kept as small as possible so that the dead space in the disposable fluid line 10 is small, such as less than 2 ml. The pressure drop in one direction across the disposable fluid line 10 is small, such as less than 40 mbar (4 kPa) at a flow rate of 300 ml/min.

[0415] Figure 21 shows an alternative version of the disposable dialysate line 10a, which is used when a sample of the patient's dialysate is to be collected. The sampling disposable dialysate line 10a comprises, in addition to the features of the normal disposable dialysate line 10, a syringe 652 which fits into a drive mechanism (not shown) in the sampling module 700. The syringe 652 draws off 15 ml of the drained dialysate. Since the dialysate is mixed within the body, the sampling may take place any time during the drain

cycle and will represents an average of the whole treatment session. The filled syringe 652 can then be broken off from the sampling disposable dialysate line 10a by means of a self-sealing frangible connection (not shown) and sent for analysis. If desired, the syringe can be visually examined to check the clarity of the dialysate.

[0416] Referring back to Figure 7, when it is desired to empty the patient's peritoneal cavity, the drained fluid is drawn through the disposable fluid line 10 to the patient drain connection 9b, through the sterilizable connector 604, and then through a patient drain cut-off valve 606. From the patient drain cut-off valve 606 the drained fluid passes through a first patient drain valve 608 and past two independent patient drain pressure sensors 610, which monitor that the negative pressure applied to the peritoneal cavity of the patient by the negative pressure drain connection 14a is not so great as to harm the patient. Downstream of the patient drain pressure sensors 610 the output volumetric flow meter 650 measures the volume of fluid removed from the patient's peritoneal cavity, and a second patient drain valve 612 is provided downstream of the volumetric flow meter 650 to close off the negative pressure drain connection 14a.

[0417] A sterilization bypass valve 614 allows a fluid path to be opened from the sterile fluid connection 8a to the negative pressure drain connection 14a without going through the patient, when a patient bypass valve 616 is open. The PD fluid can be directed directly to the ambient pressure drain connection 14b, without passing through the patient, by opening a sterilization heat recovery bypass valve 618 downstream of the patient bypass valve 616.

[0418] During filling of the patient, the pressure of the PD fluid entering the peritoneal cavity is monitored by closing the patient bypass valve 616, the sterilization bypass valve 614 and the second patient drain valve 612, and opening the first patient drain valve 608 and the patient drain cut-off valve 606. In this way the pressure at the patient's

peritoneal cavity is transmitted back from the Y-connector 646 of the disposable fluid line 10 by means of the patient pinch valve 624, the patient drain cut-off valve 606 and the first patient drain valve 608 to the patient drain pressure sensors 610, although there is no flow along this fluid path because the second patient drain valve 612 is closed. By means of this arrangement, the patient drain pressure sensors 610 can measure accurately the pressure of the fluid entering the patient's peritoneal cavity during filling thereof, because the pressure measurement is made as close to the peritoneal cavity as possible.

[0419] The pressure sensors 610 may control the drain pump 508 to start operation (and opening of valve 612) if the positive pressure becomes too large, such as more than 2 meter water pillar over atmosphere pressure, to thereby shunt a portion of the fill fluid to the waste.

[0420] A pressure conditioning chamber 660 similar to pressure conditioning chamber 510 may be provided after patient fill valve 602 as shown by broken lines in Fig 7. The operation of chamber 660 is the same as described for chamber 510.

[0421] Alternatively, the patient drain cut-off valve 606 can be closed and the patient bypass valve 616 and the sterilization bypass valve 614 can be opened, with the sterilization heat recovery bypass valve 618 closed. In this way, a pressure tap from the sterile fluid connection 8a to the patient drain pressure sensors 610 is formed, such that the patient drain pressure sensors 610 can measure the pressure of the fluid entering the peritoneal cavity of the patient along the sterile fluid connection 8a.

[0422] Monitoring of the pressure at the peritoneal cavity, enables the control system to detect whether the patient has blocked or disconnected the disposable dialysate line 10.

[0423] During sterilization of the sterilizable connector 604, hot sterilizing fluid enters the cyclor and sterilizable connector module 600 under pressure through the sterile fluid

connection 8a and passes through the patient fluid valve 602, through the sterilizable connector 604, through the patient drain cut-off valve 606, and through the sterilization bypass valve 614 to the sterilization output connection 8b. The first patient drain valve 608 is closed during sterilization to prevent the sterilizing fluid reaching the output volumetric flow meter 650, which may be damaged at the sterilization temperature, and also to prevent the patient drain pressure sensors 610 from being subjected to the high pressure required to stop the water at sterilization temperature from boiling. Flow meters and pressure sensors that have the necessary accuracy for this role and can withstand the sterilization pressure and temperature are expensive. Thus, the provision of the first patient drain valve 608 reduces the cost of the apparatus 100.

[0424] The heat from the sterilizing fluid is recovered in the thermal control and sterilization module 300 and the cooled fluid is returned to the cyclor and sterilizable connector module 600 through the sterilization fluid return connection 8c. The fluid passes to the ambient pressure drain connection 14b through a sterilization pressure release valve 620 to return the fluid to ambient pressure and through a sterilization return shut-off valve 622.

[0425] In a second sterilization route, the patient fill valve 602 is closed and the patient bypass valve 616 is opened so that sterilization fluid at high temperature and pressure can pass from the sterile fluid connection 8a to the sterilization output connection 8b via the patient bypass valve 616.

[0426] For disinfection, fluid at disinfection temperature is passed through the fluid lines of the cyclor and sterilizable connector module 600 and out through the negative pressure drain connection 14a and the ambient pressure drain connection 14b, to disinfect those components which are not sterilized.

[0427] Operation of the apparatus

[0428] The operation of the apparatus 100 as a whole will now be described. The default state of all valves is closed for most of the valves. Thus, in its initial operating mode, the inlet valve 202 of the water preparation module 200 and the thermal drain connection valve 520 and the heat recovery return valve 532 of the drainage module 500 are closed, as are the patient pinch valves 624 of the cycler and sterilizable connector module 600. In this state therefore the apparatus is sealed off from the external environment.

[0429] Initially, the concentrate disposable container 402 is not connected to the manifold 404, but the disposable fluid line 10 (with membranes 634 intact) is partially inserted in the sterilizable connector 604. All of the pumps and heaters of the apparatus are initially inoperative, and the patient output heat exchanger 314 is initially drained of water.

[0430] Disinfection of the apparatus

[0431] The first stage of operation is the disinfection of the entire fluid circuit, starting with the water preparation module 200. For disinfection, the inlet valve 202 is opened so that water can flow into the isolator 208. The isolator air vent valve 209 is open to allow air from the isolator 208 to exit to atmosphere through the isolator air vent 17. The disinfectant selection valve 256 is positioned to direct the waste flow from the second RO membrane unit 252 through the disinfectant cartridge 210 and through the disinfection valve 212, which is open. The degassing pump 222 is operative and draws fluid through the disinfection cartridge 210, or from the isolator 208 if insufficient fluid is available from the fluid path through the disinfection cartridge 210. The fluid from the disinfection cartridge 210 (or the isolator 208) passes to the thermal control and sterilization module 300 via the cooling water output 2a and is preheated by the water heater 322 before being returned to the water preparation module 200 via the cooling water return connection 2b. The fluid then passes through the degassing components, 214 through 224, which degas the fluid.

[0432] The RO pump 236 is operative to draw fluid from the degassing chamber 224 and pass the fluid through the first RO membrane unit 238. The first RO membrane bypass valve 250 is open so that waste fluid from the first RO membrane unit 238 is redirected to the output side of the RO membrane to continue the fluid path. No fluid from the first RO membrane unit 238 passes through the purification waste connection 2d, because the flow path through this connection is stopped by the thermal drain connection valve 520 in the drainage module 500. Disinfection fluid from the output side of the first RO membrane unit 238 passes through the RO pressure relief valve 260 and also past the second RO membrane unit 252 and is recirculated back to the disinfectant selection valve 256. Thus, it will be seen that a first disinfection loop is provided according to which water is circulated through the disinfection cartridge 210 to dilute the disinfectant and the diluted disinfectant is circulated through the majority of the water preparation module 200. None of the pumps in the thermal control and sterilization module 300, the concentrate mixing module 400 or the drainage module 500 are operative during the initial disinfection of the water preparation module 200. There are therefore no components that pump fluid from the purified water connection 2c, such that a negligible amount of fluid crosses the second RO membrane unit 252 because there is no pressure differential across the membrane unit 252. Any fluid which does cross the second RO membrane unit 252 is routed to the external drain connection via the purified water connection 2c, the mixing water feed connection 4a, the mixing system bypass valve 440, the mixing module output connection 4b, the OLA input valve 356, the sterile fluid connection 8a, the patient bypass valve 616, the sterilization heat recovery bypass valve 618, the ambient pressure drain connection 14b, the heat recovery drain connection 13b, the heat recovery drain return connection 13c and the open heat recovery return valve 532. This water is replaced by water from the tap water inlet 1 by means of particle filter 204 and water softener

206.

[0433] During the first phase of disinfection of the water preparation module 200, the air bleed valve 320 in the thermal control and sterilization module 300 is opened and the patient output heat exchanger pump 316 is operated to fill the patient output heat exchanger with disinfectant and to recirculate this disinfectant through the recirculation restrictor 310.

[0434] By closing the proportioning valve 214 completely with the degassing bypass valve 226 also closed, the flow through the cooling water return connection 2b is stopped. The patient output heat exchanger pump 316 is then used to pump disinfectant from the cooling water output 2a through the open air bleed valve 320, through the patient output heat exchanger vent connection 2e and into the isolator 208 to disinfect the patient output heat exchanger vent connection 2e. The isolator air vent valve 209 is closed during this process. The disinfectant from the isolator 208 continues to the cooling water output 2a of the water preparation module 200 to close this disinfectant circulation loop.

[0435] The patient output heat exchanger 314 can be drained of disinfectant by subsequently opening the isolator air vent valve 209 and the air bleed valve 320 while the patient output heat exchanger drain valve 318 is open and fluid is circulating between the cooling water output 2a and the cooling water return connection 2b when the patient output heat exchanger pump 316 is inoperative.

[0436] The air passage between the degassing chamber 224 and the isolator 208 is disinfected by closing the isolator air vent valve 209 and opening the degassing bypass valve 226. The degassing pump 222 is then operated with the RO pump 236 off such that the only flow from the degassing chamber 224 is directly to the isolator 208 through the air passage.

[0437] At the end of the disinfection process, the disinfectant selector valve 256 is returned to its default position with the first RO membrane bypass valve 250 still open. Disinfectant is circulated by the RO pump 236 past the

first RO membrane unit 238, the second RO membrane unit 252 and back round to the RO pump 236 via the second RO output restrictor 254 and the disinfectant selection valve 256. After this circulation, the first RO membrane bypass valve 250 is closed and the thermal drain connection valve 520 in the drainage module 500 is opened so that disinfectant can flow through the purification waste connection 2d to the thermal drain connection 13a and out of the external drain connection 16.

[0438] Finally, the water preparation module 200 is flushed with water to remove any remaining disinfectant along the disinfectant routes described above.

[0439] It will be seen from the above that the entire water preparation module 200 from the water softener 206 up to and including the second RO membrane unit 252 is chemically disinfected by the above process.

[0440] Downstream of the second RO membrane unit 252, water at disinfection temperature supplied from the RO membrane disinfection connection 3 is used to disinfect the fluid path between the second RO membrane unit 252 and the purified water connection 2c. In this case, water from the tap water connection 1 passes along the normal purification fluid path through the water preparation module 200 so that RO water is produced at the output side of the second RO membrane unit 252. The mixing water stop valve 442 of the concentrate mixing module 400 is opened and the salt input displacement pump 452 is energised to draw water from the mixing water feed connection 4a. The water supply to the mixing water feed connection 4a of the mixing module 400 is drawn from the purified water connection 2c of the water preparation module 200 and heated to disinfection temperature by the disinfection heater 330. The salt input displacement pump 452 pumps the water at disinfection temperature through the open RO membrane disinfection valve 499 to the output side of the second RO membrane unit 252 by means of the RO membrane disinfection connection 3. Thus, a closed recirculation loop of water at

disinfection temperature is provided, the temperature of which is monitored by the second RO temperature sensor 264.

[0441] The disinfection heat exchanger bypass valve 328 is disinfected as part of the above heat disinfection loop, by opening the valve to allow the hot disinfection water to pass there through.

[0442] The hot water is flushed to the drainage module 500 by deactivating the salt input displacement pump 452 and activating the flow control pump 446 to pump the hot water to the drainage module 500 via the mixing module drain connection 15.

[0443] Before the disposable concentrate container 402 is connected to the manifold 404, the manifold 404 and cap 406 are heat disinfected. To achieve this, the cap 406 is located on the manifold 404 to form a sealed cavity. The flow control pump 446 is activated to pump water heated to disinfection temperature by the disinfection heater 330 through the mixing water feed connection 4a. The flow control pump 446 pumps the disinfection water through the reservoir filling valve 466 and into the concentrate reservoir 468. The hot disinfecting fluid is pumped into the cavity formed by the manifold 404 and cap 406 sequentially in time through each of the reservoir vent disinfection valve 498, the reservoir output valve 470 and each of the salt input valves, 478 through 488, so that all of these valves are disinfected. The cap air vent valve 474 vents air from the cavity formed by the manifold 404 and the cap 406 to the drainage module 500 via the mixing module drain connection 15. Once the manifold 404 and cap 406 are full of hot disinfection fluid, the fluid is forced through the mixing module drain connection 15 by means of the cap air vent valve 474 to the drainage module 500.

[0444] In the drainage module 500, the hot fluid passes out of the heat recovery drain connection 13b and through the disinfection heat exchanger 326. However, the disinfection heat exchanger bypass valve 328 is open so that no heat is lost from the disinfection fluid passing through the

disinfection heat exchanger 326 and returning to the drainage module 500 by means of the heat recovery drain return connection 13c. In this way, the heat recovery drain connection 13b and the heat recovery return valve 532 are also heat disinfected.

[0445] In order to disinfect the sodium bicarbonate air vent valve 492, water at disinfection temperature from the thermal control and sterilization module 300 is drawn through the mixing water feed connection 4a by the salt input displacement pump 452. At this time, the only open fluid passages into the filled cavity formed by the manifold 404 and the cap 406 are by means of the sodium bicarbonate air vent valve 492 and the sodium bicarbonate input valve 482. Thus, as the salt input displacement pump 452 pumps hot water out of the cavity formed by the manifold 404 and the cap 406 via the sodium bicarbonate input valve 482 the hot water is replaced from the mixing water feed connection 4a by means of the sodium bicarbonate air vent valve 492. The sodium bicarbonate air vent valve 492 is toggled to disinfect the air vent and the fluid channel 428. The hot water is recirculated through this loop by closing the heat recovery return valve 532 in the drainage module 500 and opening the mixing water stop valve 442. The same method can be used to disinfect the sodium chloride air vent valve 494 and the sodium chloride input valve 484.

[0446] The fluid path to the glucose compartment 420 of the disposable concentrate container 402 is disinfected by using the flow control pump 446 to pump hot water from the thermal control and sterilization module 300 by means of the mixing water feed connection 4a through the mixing system bypass valve 440, the glucose selector valve 444 and the glucose input valve 490 into the cavity formed by the manifold 404 and the cap 406. Subsequently, with the flow control pump 446 switched off, the glucose recirculation pump 448 is used to recirculate the hot water through the glucose output channel 436 and the fluid input channel 434. The glucose input valve

490 is closed at this stage. Finally, the hot disinfection fluid can exit the cavity formed by the manifold 404 and cap 406 via the cap air vent valve 474 and the mixing module drain connection 15.

[0447] After disinfection, the manifold 404 and cap 406 are drained by connecting the cavity formed thereby to atmosphere at the air vent 6 by means of the cap air vent valve 474, and pumping the water out of the manifold and cap 406 using the salt input displacement pump 452 by means of the reservoir vent disinfection valve 498, the concentrate reservoir 468 and the reservoir output valve 470. The salt input displacement pump 452 pumps the water to the drainage module by means of the flow control pump bypass valve 458, the drain disinfection valve 464 and the mixing module drain connection 15.

[0448] In order to disinfect the thermal control and sterilization module 300 and the cyclor and sterilizable connector module 600, hot water is pumped by the volumetric pump 352 from the disinfection heater 330 by means of the mixing water feed connection 4a, the mixing system bypass valve 440 and the mixing module output connection 4b through the OLA input valve 356. In a further route, the disinfection fluid is pumped through the OLA sterilization valve 376. The disinfection fluid passes through the thermal control and sterilization module 300 to the sterile fluid connection 8a and then through the patient fill valve 602, through the chamber 632 and fluid passage 640 of the sterilizable connector 604, the patient drain cut-off valve 606, the sterilization bypass valve 614 the sterilization heat recovery bypass valve 618 and into the drainage module 500 by means of the ambient pressure drain connection 14b.

[0449] In a further disinfection route, the disinfection fluid entering the cyclor and sterilizable connector module 600 through the sterile fluid connection 8a, passes through the patient bypass valve 616, and through the sterilization heat exchanger 378 via the sterilization output connection 8b. At this time, there is no fluid flow through the other side of

the sterilization heat exchanger 378 and thus no heat is lost from the disinfection fluid during its passage through the sterilization heat exchanger 378. The disinfection fluid entering the cyclor and sterilizable connector module 600 via the sterilization fluid return connection 8c passes to the drainage module 500 via the ambient pressure drain connection 14b.

[0450] In the final disinfection route through the cyclor and sterilizable connector module 600, hot disinfection fluid from the sterile fluid connection 8a passes through the patient fill valve 602, the sterilizable connector 604, the patient drain cut-off valve 606, the first patient drain valve 608 and onward to the negative pressure drain connection 14a. At this time, the drainage pump 508 is operative.

[0451] It will be seen from the above that the whole fluid system from the water softener 206 to the patient pinch valves 624, including the drainage module 500 can be disinfected either chemically or by heat disinfection.

[0452] Cleaning and Flushing

[0453] After disinfection, the disposable concentrate container 402 is connected to the manifold 404, and a downstream cleaning operation is then carried out.

[0454] For the cleaning operation, RO water preheated by the disinfection heater 330 to mixing temperature is drawn into the concentrate mixing module 400 by the salt input displacement pump 452 through the mixing water stop valve 442 and directed through the cleaning agent input valve 480 into the cleaning agent compartment 410 of the concentrate disposable container 402. Sufficient water is pumped into the cleaning agent compartment 410 to dissolve all of the powdered cleaning agent stored therein. Once the cleaning agent is dissolved, the salt input displacement pump 452 is reversed to draw the cleaning agent solution out of the cleaning agent compartment 410 through the cleaning agent input valve 480. The cleaning agent is pumped into the concentrate reservoir 468 via the reservoir filling valve 466 by the salt input

displacement pump 452. From the concentrate reservoir 468, the cleaning agent is passed to the drainage module 500 via the reservoir air vent valve 496 and the mixing module drain connection 15.

[0455] For cleaning of the downstream components in the thermal control and sterilization module 300 and the cyclor and sterilizable connector module 600, the cleaning agent is pumped by the salt input displacement pump 452 through the flow control pump bypass valve 458 and the reservoir filling valve 466 to the mixing module output connection 4b. The flow of cleaning agent is directed through the thermal control and sterilization module 300 and the cyclor and sterilizable connector module 600 according to any of the disinfection routes described above.

[0456] After cleaning, the thermal control and sterilization module 300 and the cyclor and sterilizable connector module 600 are flushed with purified water from the water preparation module 200 to remove any remaining cleaning agent.

[0457] The cleaning agent may be sodium carbonate, but other cleaning agents may be used, such as citric acid, or precursors for a cleaning agent.

[0458] Treatment

[0459] Once the fluid system has been disinfected, cleaned and flushed, the first stage of the treatment process is the dissolution of the salts and glucose in the concentrate disposable container 402. Thus, RO water at mixing temperature is pumped by the salt input displacement pump 452 through the mixing water stop valve 442 sequentially into each of the salt compartments, 412 through 418, through the respective input valves, 482 through 488. Sufficient water is pumped by the salt input displacement pump 452 to fill the respective compartment, 412 through 418, of the concentrate disposable container 402, but the volume of fluid pumped by the salt input displacement pump 452 is carefully monitored to ensure that too much water is not input into the compartment, 412

through 418, which would overflow through the air vent channel, 424 and 428. Once each compartment, 412 through 418, is full, the respective input valve, 482 through 488, is closed while the salt dissolves. The volumes of water input into the compartments, 408 and 412 through 418, are carefully selected. Thus, the control system knows how much water is in each compartment. If too much water is introduced into the sodium bicarbonate 412 or the sodium chloride compartment 414 no harm is done because the resultant solution will still be substantially saturated.

[0460] For filling of the glucose compartment 420, RO water at mixing temperature, for example 37°C, is pumped by the flow control pump 446 from the mixing water feed connection 4a by means of the mixing system bypass valve 440, the reservoir filling valve 466 and the glucose selector valve 444 through the open glucose input valve 490 into the glucose compartment 420 by means of the fluid input channel 434. The glucose recirculation pump 448 is deactivated at this stage. Once sufficient fluid has been pumped into the glucose compartment 420 to fill that compartment to a level not exceeding the top of the glucose air vent channel 432, the glucose input valve 490 is closed and the glucose recirculation pump 448 recirculates the glucose solution to aid dissolution. The volume of water pumped into the glucose compartment 420 determines the concentration of the glucose solution.

[0461] While the glucose and salts are dissolving, the patient fluid circuit is sterilized. Thus, RO water is drawn by the volumetric pump 352 from the mixing water feed connection 4a through the mixing system bypass valve 440 and the mixing module output connection 4b and is pumped through the OLA sterilization valve 376. The water passes through the sterilization heat exchanger 378, where it is preheated, and then through the second OLA heat exchanger 362 for further preheating. The volumetric pump 352 pressurises the water to a sufficiently high pressure that the OLA heating bath 364 can raise the temperature of the water to a suitable sterilization

temperature, i.e. above 100°C, preferably above 121°C, without boiling. The heated pressurised water passes through the hot side of the second OLA heat exchanger 362 and of the first OLA heat exchanger 360. However, because there is no flow through the cold side of the first OLA heat exchanger 360, no heat is transferred from the heated pressurised water. Similarly, as the heated pressurised water passes through the patient output heat exchanger 314, no heat is transferred because the water bath in the patient output heat exchanger 314 has been drained. The heated pressurised water passes through the patient output pressure relief valve 374, which is deactivated so that there is no drop in pressure, and enters the cyclor and sterilizable connector module 600 via the sterile fluid connection 8a.

[0462] In the cyclor and sterilizable connector module 600 the heated pressurised water firstly passes through the patient fill valve 602, the sterilizable connector 604, the patient drain cut-off valve 606 and the sterilization bypass valve 614 to the sterilization output connection 8b. The first patient drain valve 608 is closed during this operation to protect the patient drain pressure sensors 610 from the elevated pressure and the output volumetric flow meter 650 from the elevated temperature. Thus, the fluid path between the first patient drain valve 608 and the drainage module 500 is not sterilized. However, this line has been disinfected and does not handle fluid which is subsequently passed to the patient, so that there is no risk to the patient. From the sterilization output connection 8b the heated pressurised water passes through the sterilization heat exchanger 378 where its temperature is reduced by heat transfer to the relatively cool water passing through the OLA sterilization valve 376. The cooled pressurised water then passes via the sterilization fluid return connection 8c through the sterilization pressure relief valve 620 which reduces the pressure to atmospheric. The cooled ambient pressure water passes through the sterilization return shut-off valve 622,

through the ambient pressure drain connection 14b and the heat recovery drain connection 13b to the disinfection heat exchanger 326 where the temperature of the water is further reduced before the water is passed to the external waste connection 16 via the heat recovery drain return connection 13c and the heat recovery return valve 532.

[0463] During a further stage of the sterilization of the cyclor and sterilizable connector module 600 the patient fill valve 602 and the sterilization bypass valve 614 are closed so that the high temperature pressurised water can pass through the patient bypass valve 616 (which is now open) to the sterilization output connection 8b to sterilize the patient bypass valve 616.

[0464] In the above manner, it is ensured that the fluid circuit from the OLA heating bath 364 to the sterilization heat exchanger 378 is sterile. The sterility is maintained throughout the treatment session.

[0465] Once the fluid path from the OLA 375 to the sterilizable connector 604 has been sterilized, sterile fluid is passed along this path continuously until the end of the treatment session to maintain sterility. The fluid may be water from the water preparation module 200 which passes from the mixing water feed connection 4a through the mixing system bypass valve 440 to the mixing module output connection 4b, through the OLA 375, where it is sterilized and then through the patient bypass valve 616 and the sterilization heat recovery bypass valve 618 to the drainage module 500. Alternatively, the fluid may be PD fluid from the concentrate mixing module 400 which is sterilized in the OLA 375 and passed to the drainage module 500 along the same fluid path as described above. In this way, the OLA 375 can operate continuously without overheating to ensure sterility at all times. When the PD fluid is to be delivered to the patient, the patient bypass valve 616 is shut and the patient fill valve 602 is opened to allow the PD fluid to pass to the sterilizable connector 604.

[0466] Once the sterilization operation has been completed, the concentrated PD fluid is mixed in the concentrate reservoir 468 in the manner described in detail above in relation to the concentrate mixing module 400.

[0467] While the concentrated PD fluid is being mixed, the water bath of the patient output heat exchanger 314 is filled by opening the air bleed valve 320 and activating the patient output heat exchanger pump 316, in preparation for delivery of PD fluid to the patient.

[0468] The apparatus is now ready for the arrival of the patient. When the patient arrives, the membranes 634 on the disposable fluid line 10 are pierced by the sterilizable connector 604. The disposable fluid line 10 is primed by pumping PD fluid (or sterile water) from the mixing module output connection 4b through the OLA input valve 356 using the volumetric pump 352. The PD fluid is produced in the mixing module 400 by diluting the concentrated PD fluid pumped by the salt input displacement pump 452 from the concentrate reservoir 468 to the mixing chamber 450 with a flow of purified water from the water preparation module 200. The flow control pump 446 is bypassed during delivery of the PD fluid by opening the flow control pump bypass valve 458. The PD fluid passes through the first OLA heat exchanger 360, the second OLA heat exchanger 362 and the OLA heating bath 364 and is thereby sterilized. The sterilized PD fluid is brought down to the required patient temperature by the patient output heat exchanger 314 and is depressurised by the patient output pressure relief valve 374. The sterile PD fluid is then passed through the patient fill valve 602 and the patient pinch valve 624 into the disposable dialysate line 10. The PD fluid passes through the disposable fluid line 10 and returns to the sterile connector 604 via the second patient pinch valve 624. The returned fluid passes through the patient drain cut-off valve 606 and the first patient drain valve 608. The output volumetric flow meter 650 registers the fluid flow and confirms that the disposable fluid line 10 has been

successfully primed with PD fluid. The PD fluid then passes to the drainage module 500 via the negative pressure drain connection 14a. In this way, it is ensured that there is only a minimal amount of air in the disposable dialysate line which connects to the patient's peritoneal cavity.

[0469] Once the disposable fluid line 10 has been primed, the patient is invited to connect to the disposable fluid line 10 so that any fluid in the patient's peritoneal cavity can be drained. During draining of the patient the drainage pump 508 is activated to draw dialysate from the sterilizable connector 604 through the patient drain cut-off valve 606 and past the output volumetric flow meter 650 to the negative pressure drain connection 14a. The output volumetric flow meter 650 records the volume of dialysate withdrawn from the patient's cavity. During drainage, a sample of the patient's dialysate may be taken by the sampling module 700.

[0470] In the case of subsequent filling and draining of the patient's cavity, additional concentrated PD fluid is mixed by the mixing module 400 in the concentrate reservoir 468 while the patient is being drained by the cyclor and sterilizable connector module 600 and the drainage module 500.

[0471] When the patient's peritoneal cavity is empty, which is registered by a drop in pressure or flow rate detected by the patient drain pressure sensor 610 or the output volumetric flow meter 650, or when a predetermined drain time has elapsed, the drainage pump 508 is deactivated. The patient's peritoneal cavity can then be filled with sterile PD fluid from the sterile fluid connection 8a of the thermal control and sterilization module 300 by means of the patient fill valve 602, the sterilizable connector 604 and the patient pinch valve 624. During filling of the patient, the pressure of the PD fluid entering the patient is monitored using the pressure tap described in detail above in relation to the cyclor and sterilizable connector module 600. The volume of PD fluid entering the patient's peritoneal cavity is recorded by the input volumetric flow meter 350.

[0472] Once sufficient fluid has been passed to the patient, the fluid system downstream of the mixing module output connection 4b is flushed through to the drainage module 500 firstly with the remaining PD fluid (which is sterilized) and then with sterilized water to remove any glucose deposits that remain in the OLA 375 and would caramelize. The system then awaits drainage of the patient. Thus, a cycle of drains and fills can be repeated over an extended period to complete a treatment session.

[0473] At the end of a treatment session, once the patient has disconnected from the apparatus 100, any remaining salt or glucose solutions in the concentrate disposable container 402 are pumped to the drainage module by means of the mixing module drain connection 15. The fluid system is then flushed with clean water utilising the disinfection routes described above. The concentrate disposable container 402 and the disposable fluid line 10 are replaced. Finally, the system is cleaned as described above and then flushed with clean water, before the system is shut by closing the inlet valve 202, the thermal drain connection valve 520 and the heat recovery return valve 532. The apparatus is then ready for the next treatment session.

[0474] During extended periods of non-use, the entire fluid system may be filled by an engineer with a suitable preservative and closed to atmosphere to prevent bacteriological build-up.

[0475] It is mentioned that the apparatus has a memory device capable of storing information for later retrieval. Such a memory device may be a hard disk or a solid state memory device. Parameters to be stored in a technical log may be selected from the following non-exhaustive list: time and result of processes, like cleaning, sterilization, verification of sterility; flow rates; conditions of valves, pumps; pump speeds; sensor values such as conductivities, temperatures, pressures, temperatures.

[0476] It will be apparent to those skilled in the art that

various modifications and variations can be made to the structure and methodology of the present invention without departing from the scope or spirit of the invention. For example, certain aspects of the structure and methodology of the invention which have been particularly described in relation to peritoneal dialysis could be used for acute dialysis, home dialysis, chronic dialysis in general including hemodialysis or hemofiltration or hemodiafiltration or any other medical fluid production or treatment procedure (including producing nutritional solutions) especially those involving infusion and/or removal of fluids to and/or from a patient. Thus, it should be understood that the present invention is not limited to the examples discussed in this specification and shown in the drawings. Rather, the invention is intended to cover modifications and variations provided they come within the scope of the following claims and their equivalents.

[0477] Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention as defined by the appended claims.

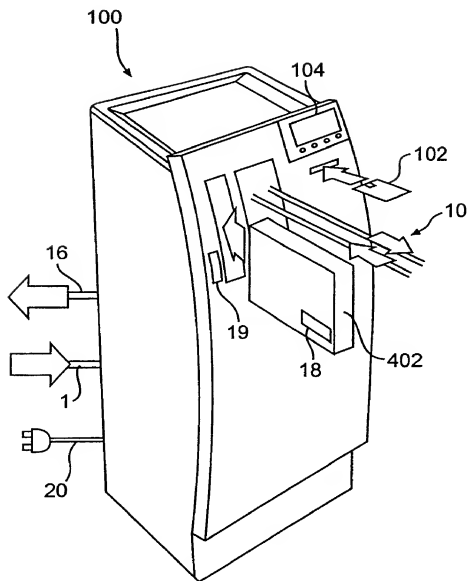
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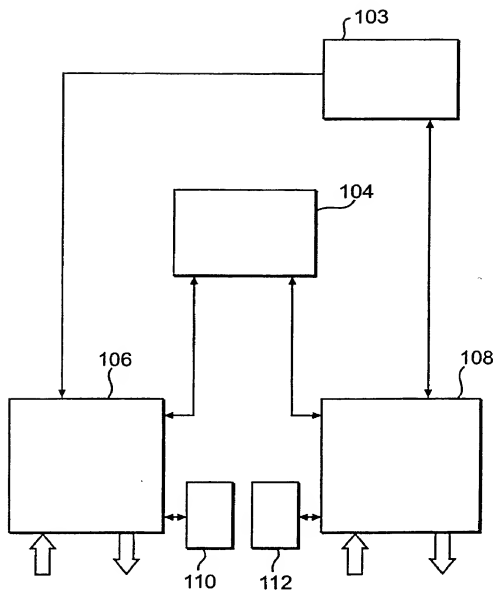
ABSTRACT OF THE DISCLOSURE

Containers for preparing peritoneal dialysis fluid, as well as methods and apparatus for doing so, are provided. The container includes a plurality of chambers and a corresponding plurality of concentrates for the peritoneal dialysis fluid, at least one of the concentrates being in the form of a powder. The methods and apparatus also provide for the preparation of selectively personalized dialysis fluid at the site of actual patient treatment.

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**FIG. 1**

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**FIG. 1a**

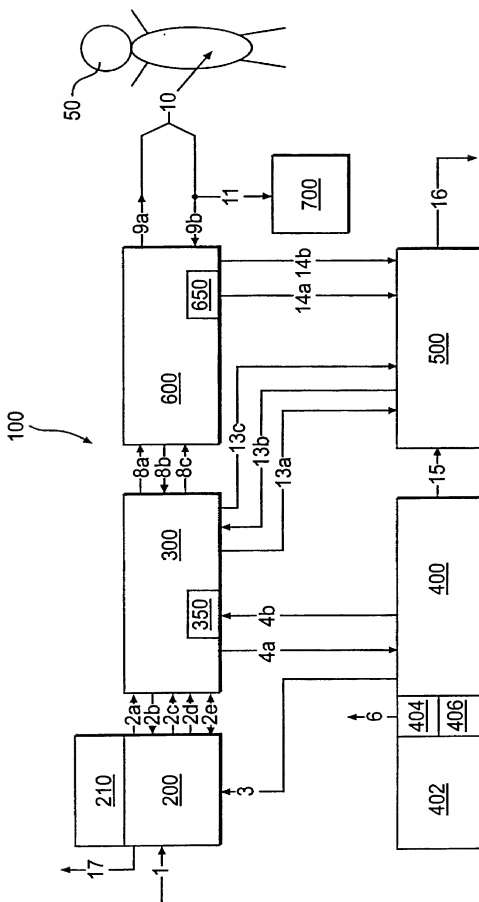


FIG. 2

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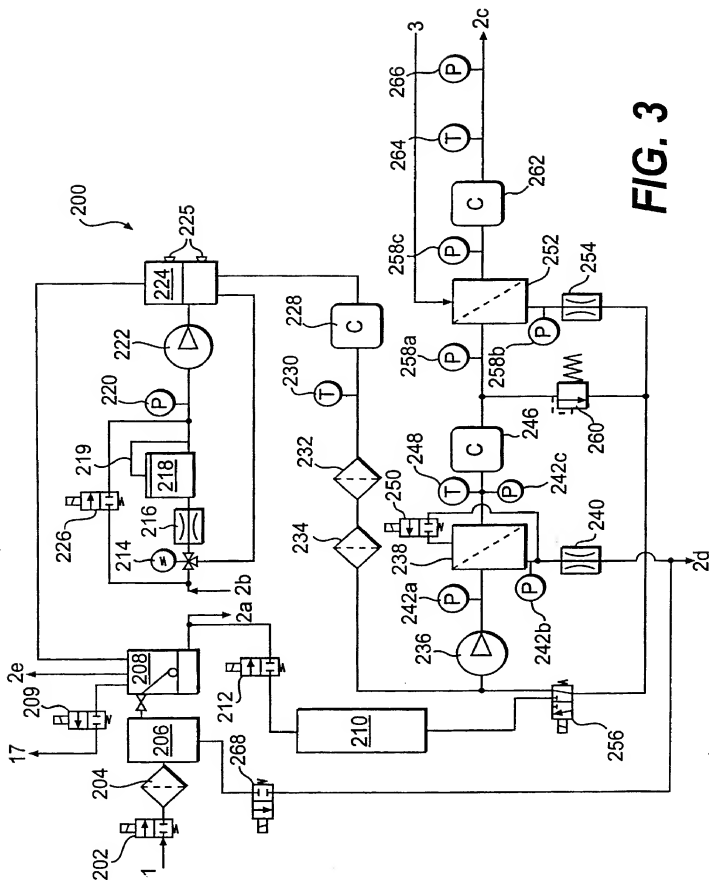
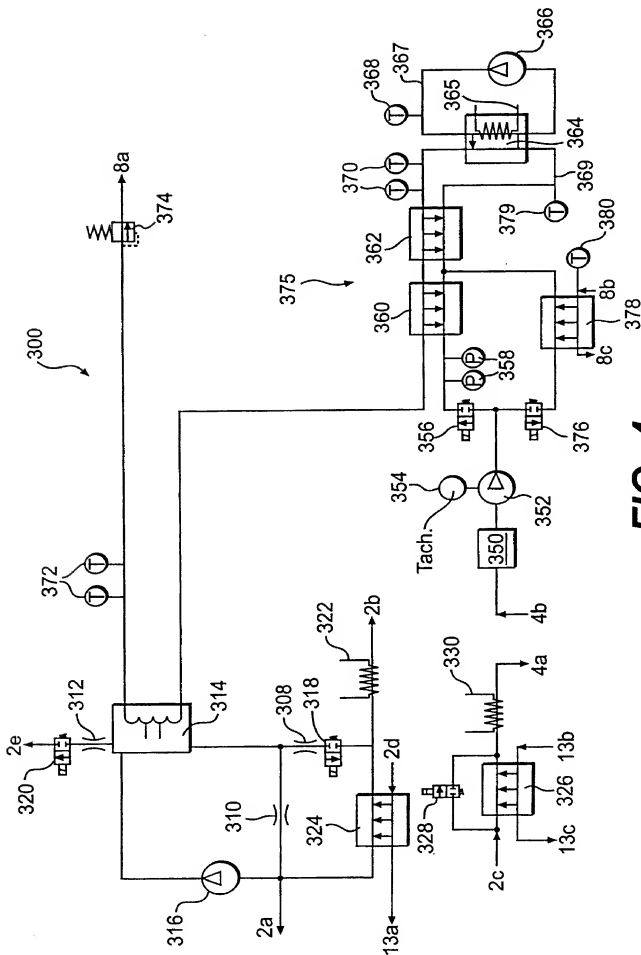


FIG. 3

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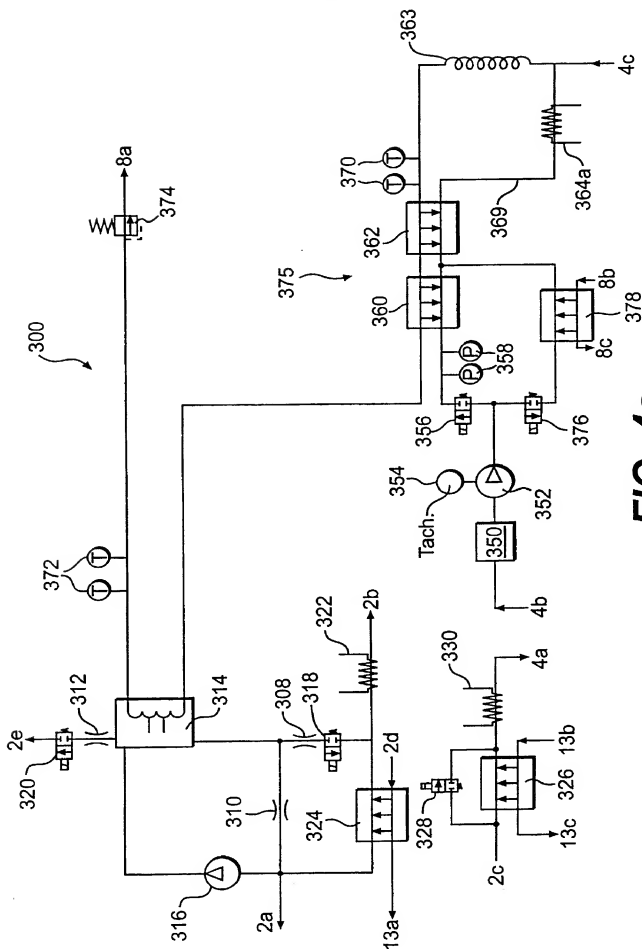


FIG. 4a

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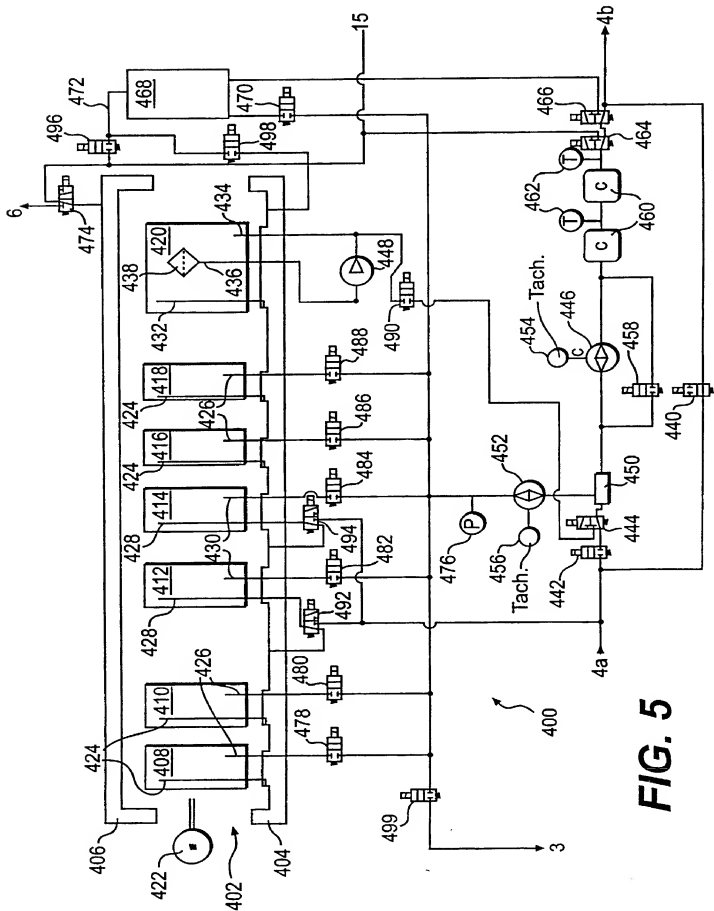


FIG. 5

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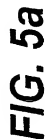
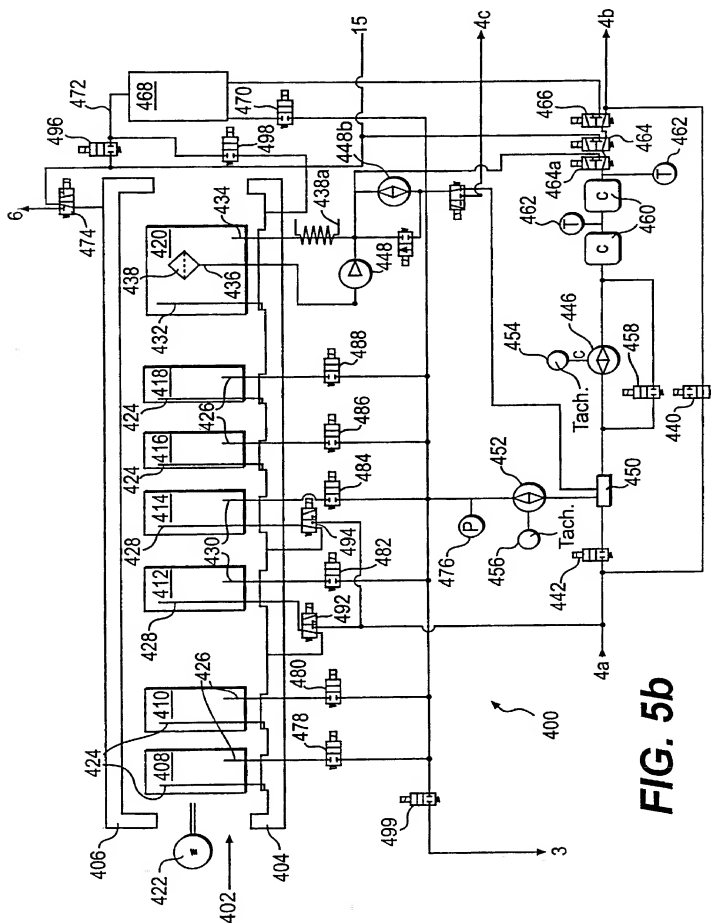
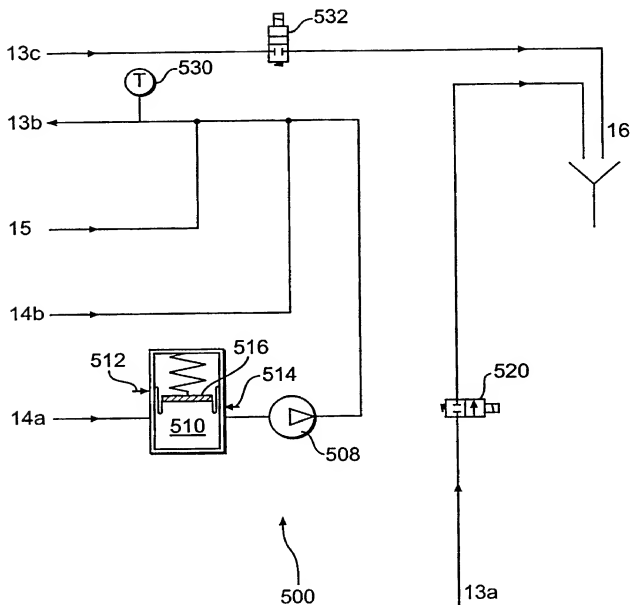


FIG. 5a

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**FIG. 6**

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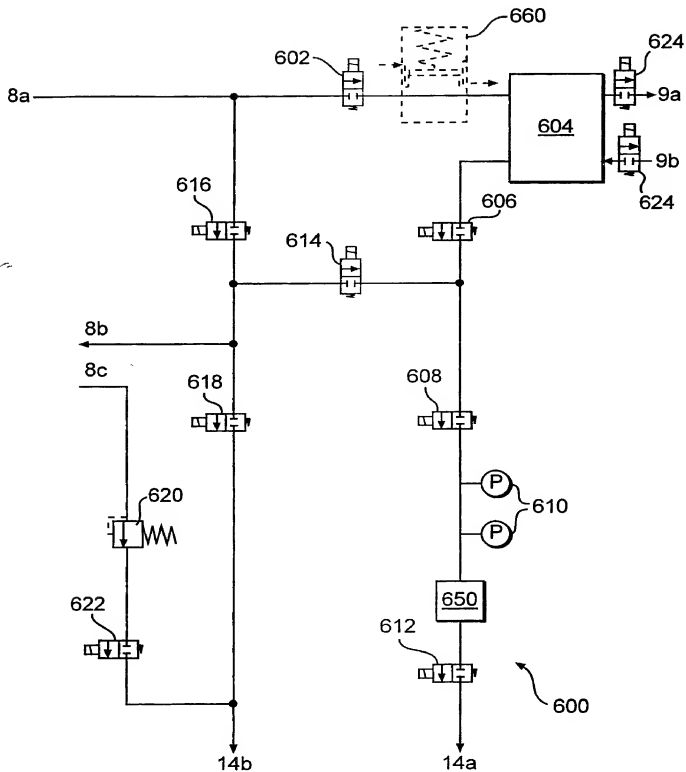
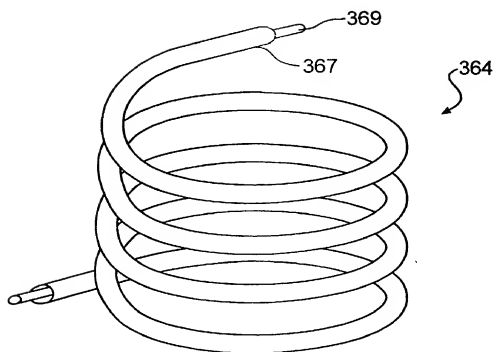
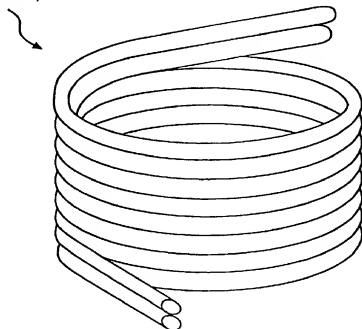


FIG. 7

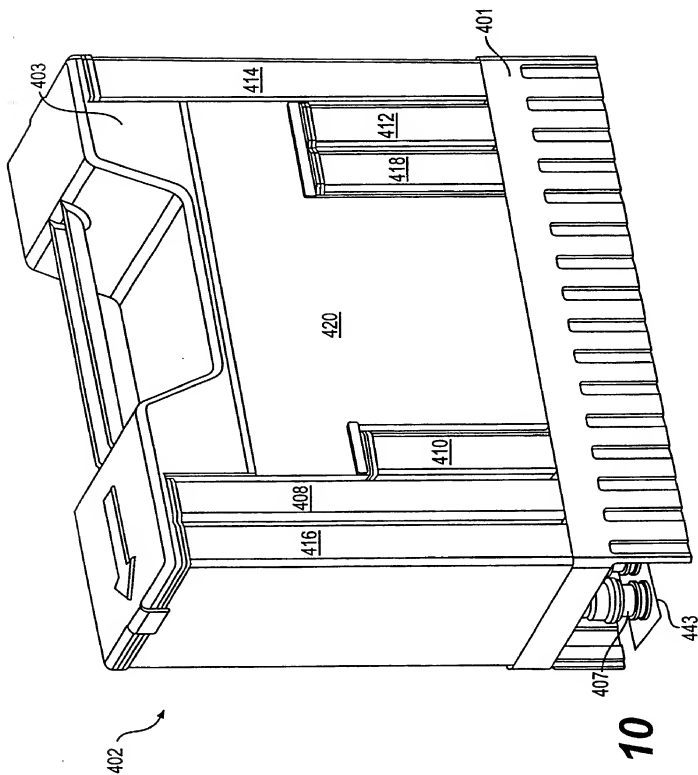
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**FIG. 8**

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**FIG. 9**

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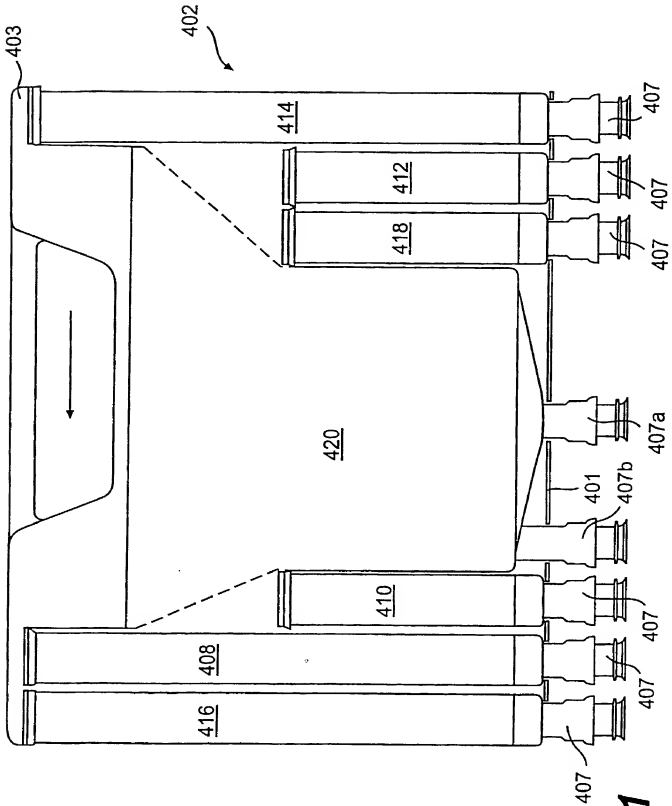
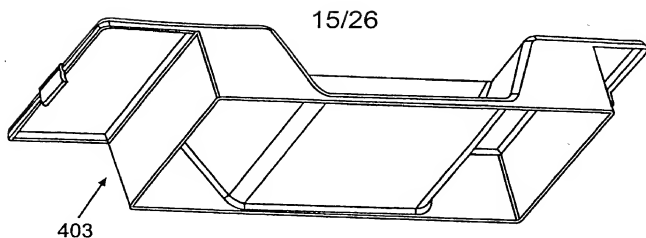
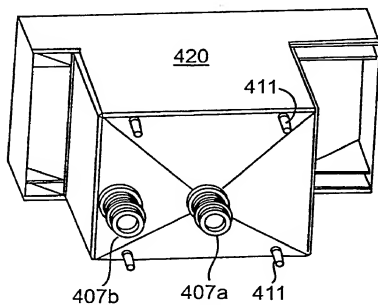
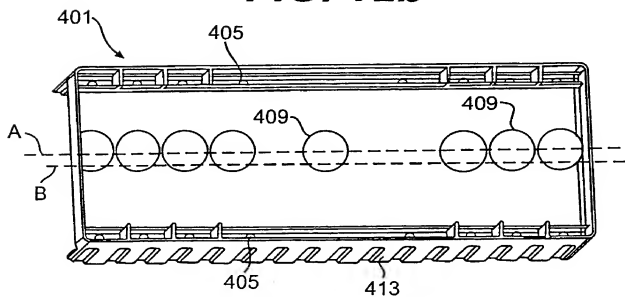
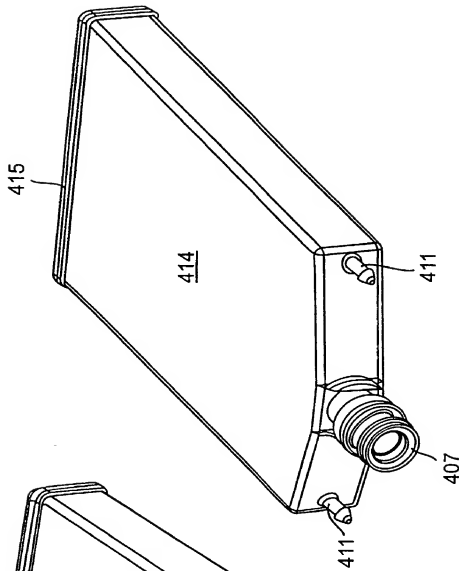
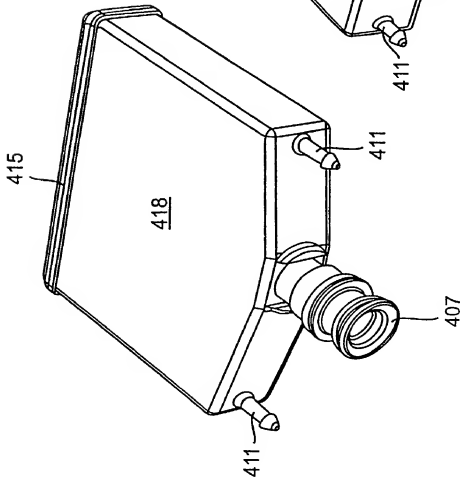


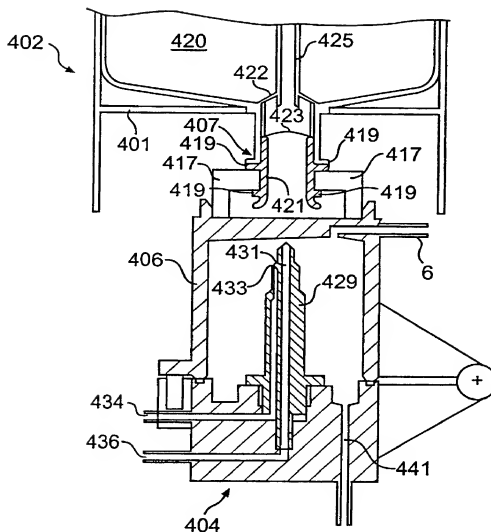
FIG. 11

**FIG. 12a****FIG. 12b****FIG. 12c**

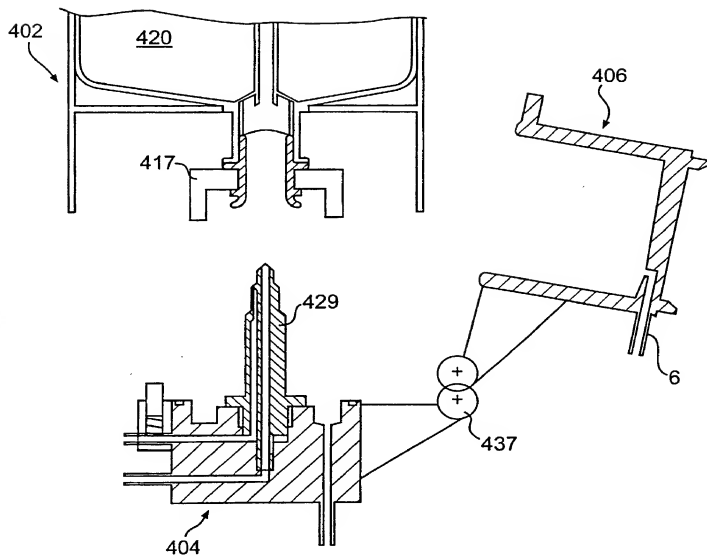
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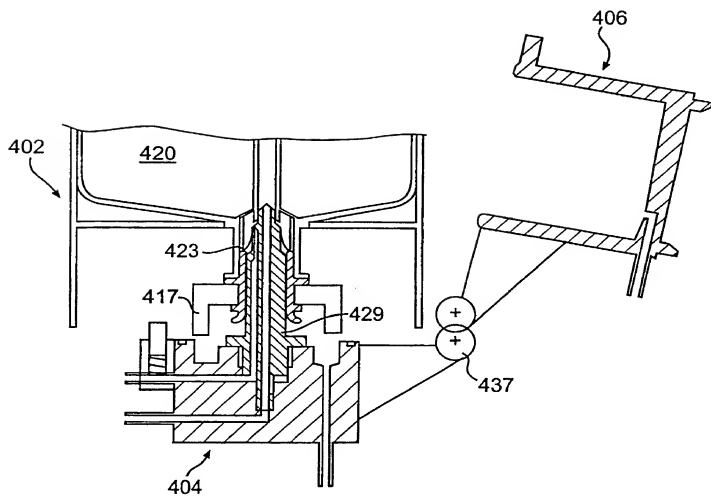
**FIG. 14****FIG. 13**

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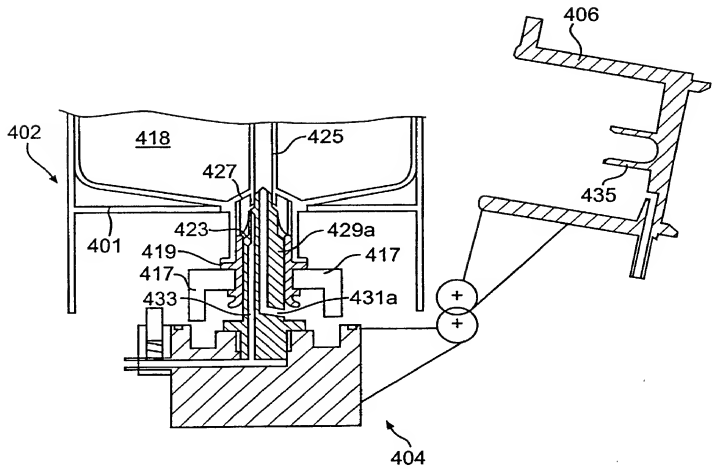
**FIG. 15**

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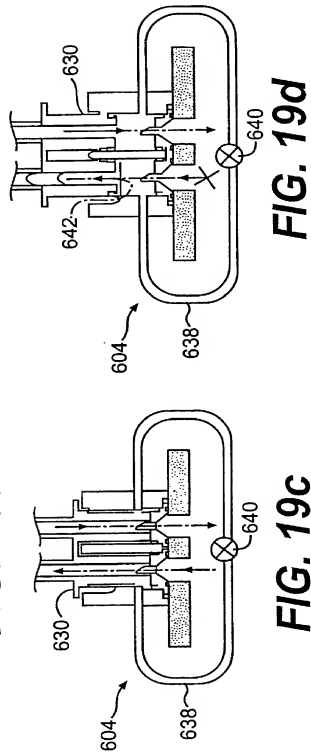
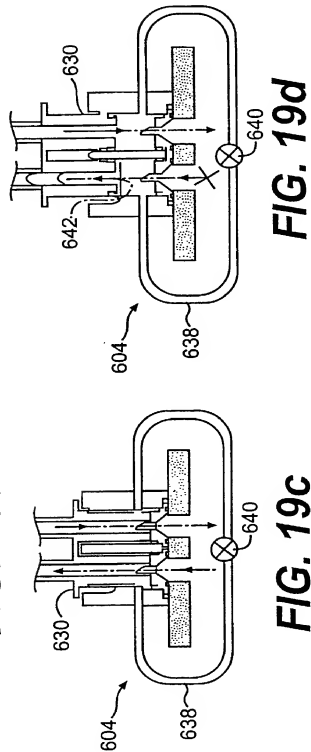
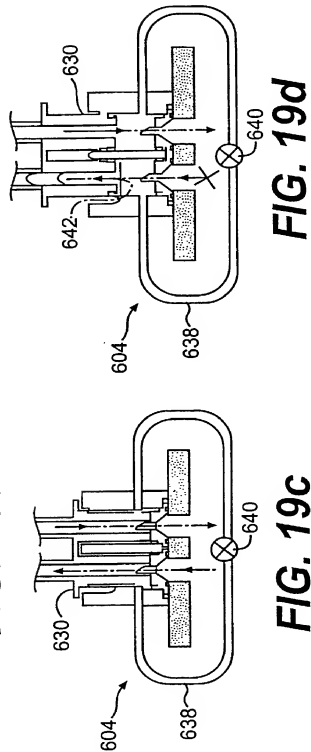
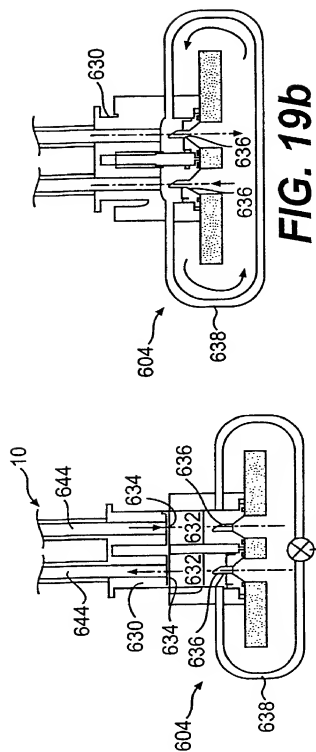
**FIG. 16**

**FIG. 17**

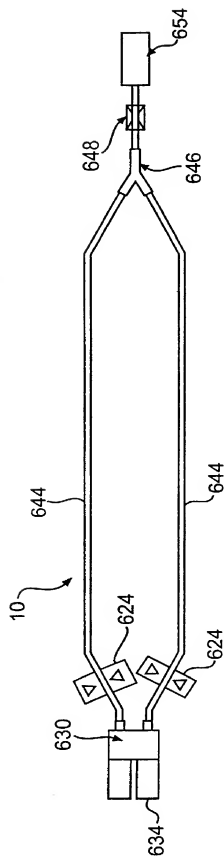
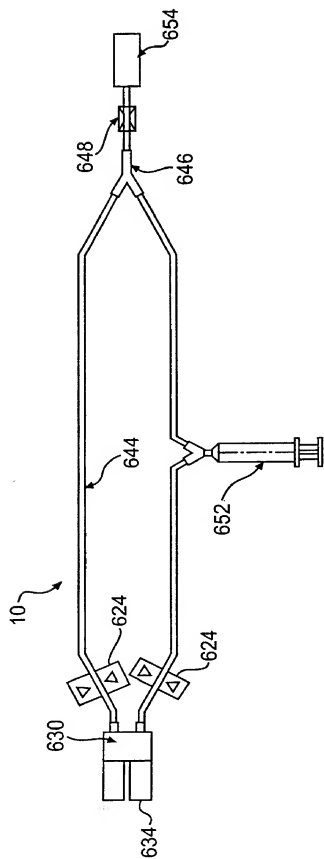
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**FIG. 18**

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**FIG. 20****FIG. 21**

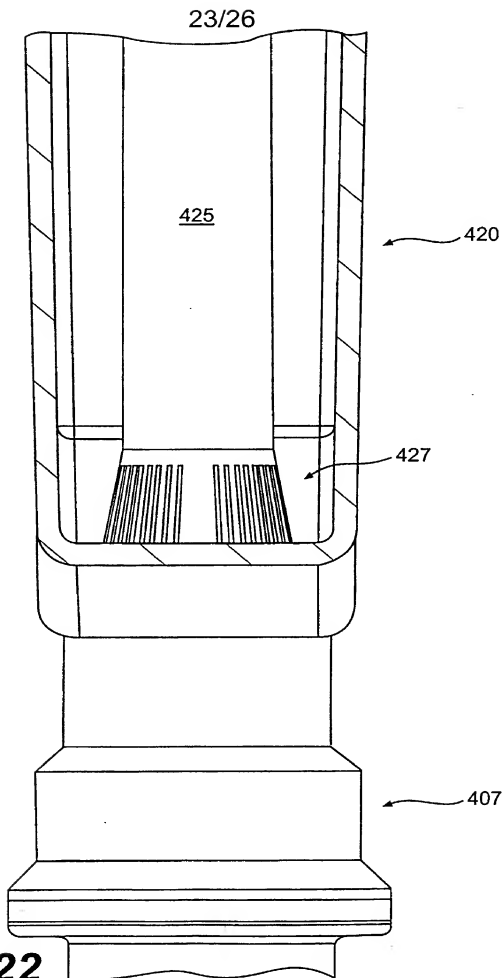
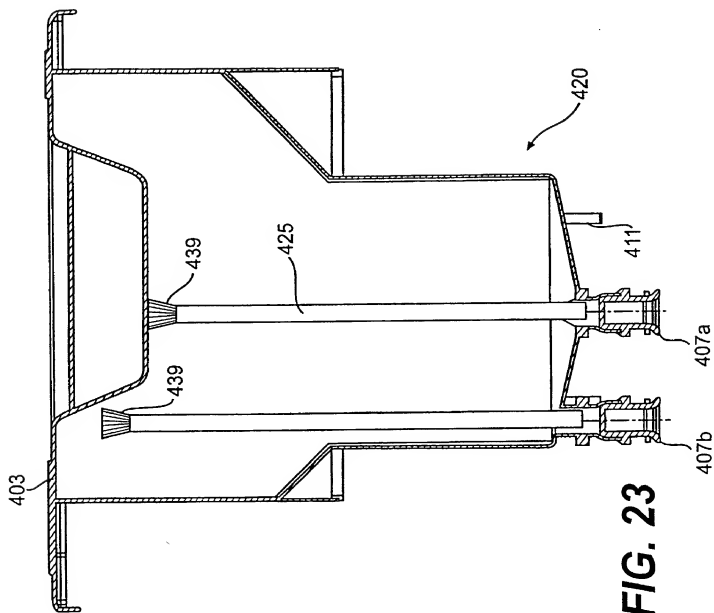
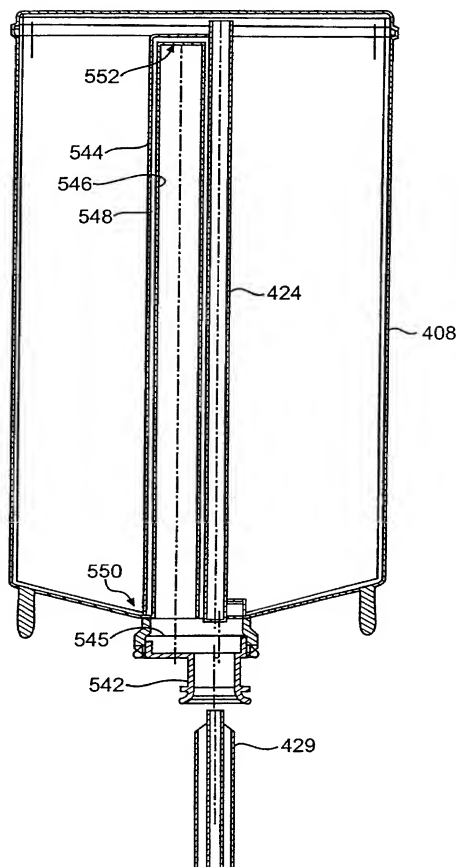


FIG. 22

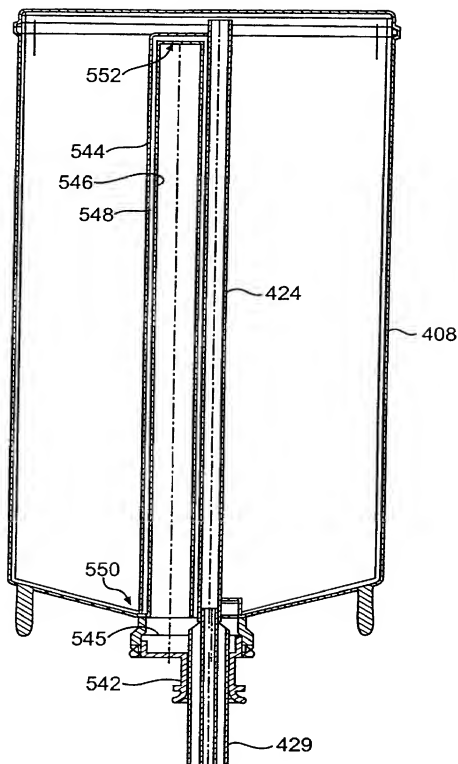
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**FIG. 24**

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**FIG. 25**

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DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION (37 CFR 1.63)	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%;">Attorney Docket Number</td> <td>GAMBRO-257</td> </tr> <tr> <td>First Named Inventor</td> <td>Olof Jansson</td> </tr> <tr> <td colspan="2" style="text-align: center;">COMPLETE IF KNOWN</td> </tr> <tr> <td>Application Number</td> <td>09/937,990</td> </tr> <tr> <td>Filing Date</td> <td></td> </tr> <tr> <td>Group Art Unit</td> <td>N/A</td> </tr> <tr> <td>Examiner Name</td> <td>Not Yet Assigned</td> </tr> </table>	Attorney Docket Number	GAMBRO-257	First Named Inventor	Olof Jansson	COMPLETE IF KNOWN		Application Number	09/937,990	Filing Date		Group Art Unit	N/A	Examiner Name	Not Yet Assigned									
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Filing Date																								
Group Art Unit	N/A																							
Examiner Name	Not Yet Assigned																							
<div style="display: flex; justify-content: space-between; align-items: flex-start;"> <div style="width: 45%;"> <input type="checkbox"/> Declaration Submitted with Initial Filing </div> <div style="width: 10%; text-align: center;">OR</div> <div style="width: 45%;"> <input checked="" type="checkbox"/> Declaration Submitted after Initial Filing (surcharge (37 CFR 1.16 (e)) required) </div> </div>																								
<p>As a below named inventor, I hereby declare that:</p> <p>My residence, mailing address, and citizenship are as stated below next to my name.</p> <p>I believe I am the original and first inventor of the subject matter which is claimed and for which a patent is sought on the invention entitled:</p> <div style="border: 1px solid black; padding: 10px; margin: 10px 0; text-align: center;"> <p>METHOD, APPARATUS AND COMPONENTS OF DIALYSIS SYSTEM</p> <p><small>(Title of the Invention)</small></p> </div> <p>the specification of which</p> <div style="display: flex; align-items: center;"> <input type="checkbox"/> is attached hereto <div style="margin: 0 10px;">OR</div> <input checked="" type="checkbox"/> was filed on (MM/DD/YYYY) 03/30/2000 as United States Application Number or PCT International Application No. PCT/SE00/00615 and was amended on (MM/DD/YYYY) (if applicable). </div> <p>I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.</p> <p>I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR 1.56, including for continuation-in-part applications, material information which became available between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.</p> <p>I hereby claim foreign priority benefits under 35 U.S.C. 119(a)-(d) or (f), or 365(b) of any foreign application(s) for patent, inventor's or plant breeder's rights certificate(s), or 365 (a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent, inventor's or plant breeder's rights certificate(s), or of any PCT international application having a filing date before that of the application on which priority is claimed.</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th rowspan="2">Prior Foreign Application Number(s)</th> <th rowspan="2">Country</th> <th rowspan="2">Foreign Filing Date (MM/DD/YYYY)</th> <th rowspan="2">Priority Not Claimed</th> <th colspan="2">Certified Copy Attached?</th> </tr> <tr> <th>YES</th> <th>NO</th> </tr> </thead> <tbody> <tr> <td rowspan="4">9901165-2</td> <td rowspan="4">SE</td> <td rowspan="4">03/30/1999</td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </tbody> </table> <div style="margin-top: 10px;"> <input type="checkbox"/> Additional foreign application numbers are listed on a supplemental priority data sheet PTO/SB/02B attached hereto: </div>		Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?		YES	NO	9901165-2	SE	03/30/1999	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Prior Foreign Application Number(s)	Country					Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached?																
		YES	NO																					
9901165-2	SE	03/30/1999	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>																			
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																			
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																			
			<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>																			

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001 and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

NAME OF SOLE OR FIRST INVENTOR:



A petition has been filed for this unsigned inventor

Given Name
(first and middle (if any))

Olof

Family Name
or Surname

Jansson

Inventor's
Signature

Date

16/11 - 2001

Residence: City

Vellinge

State

SEX

Country

Sweden

Citizenship

Sweden

Mailing
Address:

Näktergalsgatan 33

City

Vellinge

State

ZIP

S-235 38

Country

Sweden

NAME OF SECOND INVENTOR:



A petition has been filed for this unsigned inventor

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(first and middle (if any))

Jörgen

Family Name
or Surname

Jansson

Inventor's
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Date

16 NOV. 2001

Residence: City

Sjöbo

State

SEX

Country

Sweden

Citizenship

Sweden

Mailing
Address:

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City

Sjöbo

State

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S-275 00

Country

Sweden



Additional inventors are being named on the 7 supplemental Additional Inventor(s) sheet(s) PTO/SB/02A attached hereto.

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 ADDITIONAL INVENTOR(S)
 Supplemental Sheet
 Page 1 of 7

Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) <u>Lennart</u>		Family Name or Surname <u>Jönsson</u>	
Inventor's Signature <u>[Signature]</u>		Date <u>16/6 2001</u>	
Residence: City <u>Furulund</u>	State <u>SEK</u>	Country <u>Sweden</u>	Citizenship
Mailing Address: <u>Ägovägen 7</u>			
City <u>Furulund</u>	State	ZIP <u>S-244 66</u>	Country <u>Sweden</u>
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) <u>Sven</u>		Family Name or Surname <u>Jönsson</u>	
Inventor's Signature <u>[Signature]</u>		Date <u>2001-7/DEC</u>	
Residence: City <u>Staffanstorp</u>	State <u>SEK</u>	Country <u>Sweden</u>	Citizenship <u>Sweden</u>
Mailing Address: <u>Poppelvägen 8</u>			
City <u>Staffanstorp</u>	State	ZIP <u>S-245 44</u>	Country <u>Sweden</u>
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) <u>Eddie</u>		Family Name or Surname <u>Nilsson</u>	
Inventor's Signature <u>[Signature]</u>		Date <u>16 NOV. 2001</u>	
Residence: City <u>Sösådal</u>	State <u>SEK</u>	Country <u>Sweden</u>	Citizenship <u>Sweden</u>
Mailing Address: <u>Trastvägen 6</u>			
City <u>Sösådal</u>	State	ZIP <u>S-280 10</u>	Country <u>Sweden</u>
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) <u>Gerhard</u>		Family Name or Surname <u>Riede</u>	
Inventor's Signature <u>[Signature]</u>		Date <u>2001-12-18</u>	
Residence: City <u>Vellinge</u>	State <u>SEK</u>	Country <u>Sweden</u>	Citizenship <u>Sweden</u>
Mailing Address: <u>Möllerängsgatan 7</u>			
City <u>Vellinge</u>	State	ZIP <u>S-235 00</u>	Country <u>Sweden</u>

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Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))		Perry		Family Name or Surname	
Inventor's Signature		Asbrink		Date	
Malmö		Sweden		14/11/2001	
Residence: City		State SEX		Citizenship	
Malmö		Sweden		Sweden	
Mailing Address:		Lindeborgsgatan 10			
City		State		ZIP	
Malmö		S-215 82		Sweden	
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))		Jacques		Family Name or Surname	
Inventor's Signature		Chevallet		Date	
Sérézín Du Rh		France		January 14, 2002	
Residence: City		State FRX		Citizenship	
Sérézín du Rhône		France		France	
Mailing Address:		8, route de Ternay			
City		State		ZIP	
Sérézín du Rhône		F-69360		France	
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))		Thierry		Family Name or Surname	
Inventor's Signature		Court		Date	
Villeurbanne		France		14/01/2002	
Residence: City		State FRX		Citizenship	
Villeurbanne		France		France	
Mailing Address:		2, place Wilson			
City		State		ZIP	
Villeurbanne		F-69100		France	
Name of Additional Joint Inventor, if any:				<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))		Alain		Family Name or Surname	
Inventor's Signature		Faugier		Date	
Tignieu		France		January 16th 2002	
Residence: City		State FRX		Citizenship	
Tignieu		France		France	
Mailing Address:		89, avenue du Grand Paradis			
City		State		ZIP	
Tignieu		F-38230		France	

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ADDITIONAL INVENTOR(S)

Supplemental Sheet

Page 3 of 7

Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) <u>Hiram</u>		Family Name or Surname <u>Rada</u>	
Inventor's Signature <u>HIRAM RADA</u>		Date <u>January 10th 2002</u>	
Residence: City <u>Lyon</u>	State <u>FRX</u>	Country <u>France</u>	Citizenship <u>France</u>
Mailing Address: <u>4, route de Vienne</u>			
City <u>Lyon</u>	State	ZIP <u>F-69007</u>	Country <u>France</u>
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) <u>Jean-Louis</u>		Family Name or Surname <u>Romarie</u>	
Inventor's Signature <u>Jean-Louis Romarie</u>		Date <u>January 10th 2002</u>	
Residence: City <u>Décines Charpieu</u>	State <u>FRX</u>	Country <u>France</u>	Citizenship <u>France</u>
Mailing Address: <u>33-1, rue Antoine Lumière</u>			
City <u>Décines Charpieu</u>	State	ZIP <u>F-69150</u>	Country <u>France</u>
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) <u>Nicholas John</u>		Family Name or Surname <u>Kerry</u>	
Inventor's Signature		Date	
Residence: City <u>Cambridgeshire</u>	State	Country <u>United Kingdom</u>	Citizenship <u>United Kingdom</u>
Mailing Address: <u>22 Newmarket Road Burwell</u>			
City <u>Cambridgeshire</u>	State	ZIP <u>CB5 0AE</u>	Country <u>United Kingdom</u>
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any)) <u>Charles Peter</u>		Family Name or Surname <u>Bell</u>	
Inventor's Signature		Date	
Residence: City <u>Cambridge</u>	State	Country <u>United Kingdom</u>	Citizenship <u>United Kingdom</u>
Mailing Address: <u>215 Milton Road</u>			
City <u>Cambridge</u>	State	ZIP <u>CB4 1XG</u>	Country <u>United Kingdom</u>

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Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A position has been filed for this assigned inventor	
Given Name (first and middle if any)	Hiram	Family Name or Surname	Rada
Inventor's Signature		Date	
Residence: City	Lyon	State	France
Country	France	Citizenship	France
Mailing Address:	4, route de Vienne		
City	Lyon	State	F-69007
Country	France	ZIP	
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A position has been filed for this assigned inventor	
Given Name (first and middle if any)	Jean-Louis	Family Name or Surname	Ramirez
Inventor's Signature		Date	
Residence: City	Décines Charpieu	State	France
Country	France	Citizenship	France
Mailing Address:	33-1, rue Antoine Lumière		
City	Décines Charpieu	State	F-69150
Country	France	ZIP	
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A position has been filed for this assigned inventor	
Given Name (first and middle if any)	Nicholas John	Family Name or Surname	Kony
Inventor's Signature		Date	10 June 2002
Residence: City	Cambridgeshire	State	GBX
Country	United Kingdom	Citizenship	United Kingdom
Mailing Address:	22 Newmarket Road Burwell		
City	Cambridgeshire	State	GBX
Country	United Kingdom	ZIP	CB5 0AE
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A position has been filed for this assigned inventor	
Given Name (first and middle if any)	Charles Peter	Family Name or Surname	Bell
Inventor's Signature		Date	22 MAY 2002
Residence: City	Cambridge	State	GBX
Country	United Kingdom	Citizenship	United Kingdom
Mailing Address:	215 Milton Road		
City	Cambridge	State	GBX
Country	United Kingdom	ZIP	CB4 1XD

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Supplemental Sheet
Page 3 of 7

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Hiram

Family Name
or Surname

Rada

Inventor's
Signature

Lyon

Date

Residence: City

State

Country France

Citizenship France

Mailing
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City

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State

ZIP

F-69007

Country

France

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Jean-Louis

Family Name
or Surname

Romeire

Inventor's
Signature

Décines Charpieu

Date

Residence: City

State

Country France

Citizenship France

Mailing
Address:

33-1, rue Antoine Lumière

City

Décines Charpieu

State

ZIP

F-69150

Country

France

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Nicholas John

Family Name
or Surname

Kerry

Inventor's
Signature

Cambridgeshire

Date

Residence: City

State

Country United Kingdom

Citizenship United Kingdom

Mailing
Address:22 Newmarket Road
Burwell

City

Cambridgeshire

State

ZIP

CB5 0AE

Country

United Kingdom

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Charles Peter

Family Name
or Surname

Bell

Inventor's
Signature

Cambridge

Date

22 MAY 2002

Residence: City

State

GBX

Country United Kingdom

Citizenship United Kingdom

Mailing
Address:

215 Milton Road

City

Cambridge

State

ZIP

CB4 1XG

Country

United Kingdom

May, 14, 2002 2:20PM

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09937296 No. 5640-1702

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ADDITIONAL INVENTOR(S)

Supplemental Sheet

Page 4 of 7

Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))	Roger William	Family Name or Surname	Clarke
Inventor's Signature	<i>[Signature]</i>	Date	21/5/02
Residence: City	Cambridgeshire	State	GBX
Country	United Kingdom	Citizenship	United Kingdom
Mailing Address:	1A Winders Lane Histon		
City	Cambridgeshire	State	GBX
ZIP	CB4 9EZ	Country	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))	Michael John	Family Name or Surname	Dunkley
Inventor's Signature	<i>[Signature]</i>	Date	16/5/02
Residence: City	Cambridge	State	GBX
Country	United Kingdom	Citizenship	United Kingdom
Mailing Address:	13 Cockburn Street		
City	Cambridge	State	GBX
ZIP	CB1 3NB	Country	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))	Raymond Anthony	Family Name or Surname	Edgson
Inventor's Signature	<i>[Signature]</i>	Date	17/5/02
Residence: City	Litlington	State	GBX
Country	United Kingdom	Citizenship	United Kingdom
Mailing Address:	Ramscroft, Malling Lane Litlington, Nr. Royston		
City	Hertfordshire	State	GBX
ZIP	SG8 0QT	Country	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))	Peter Alan	Family Name or Surname	Evans
Inventor's Signature	<i>[Signature]</i>	Date	21 st MAY 2002
Residence: City	Cambridge	State	GBX
Country	United Kingdom	Citizenship	United Kingdom
Mailing Address:	45 Parsonage Lane Burwell		
City	Cambridgeshire	State	GBX
ZIP	CB5 0EN	Country	United Kingdom

May 14, 2002 2:20PM

LERNER DAVID LITTENBERG

0993789 No. 6046-7302

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ADDITIONAL INVENTOR(S)

Supplemental Sheet

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Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Andrew James

Family Name
or Surname

Flack

Inventor's
Signature

Cambridgeshire

Date

Residence: City

State

GBX

United Kingdom

Citizenship

United Kingdom

Mailing
Address:128 Limes Road
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City

Cambridgeshire

State

ZIP

CB3 7XU

Country

United Kingdom

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Christopher James Newton

Family Name
or Surname

Fryer

Inventor's
Signature

Cambridge

Date

Residence: City

State

United Kingdom

Citizenship

United Kingdom

Mailing
Address:149, High Street
Cottenham

City

Cambridge

State

ZIP

CB4 8SD

Country

United Kingdom

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Jonathan Randall

Family Name
or Surname

Garnsworthy

Inventor's
Signature

Cambridge

Date

21 May 2002

Residence: City

State

GBX

United Kingdom

Citizenship

United Kingdom

Mailing
Address:

100 Tenison Road

City

Cambridge

State

ZIP

CB1 2DW

Country

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Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Ian Michael Daines

Family Name
or Surname

Gaylor

Inventor's
Signature

Cambridgeshire

Date

Residence: City

State

United Kingdom

Citizenship

Mailing
Address:24 Willow Lane
Cambourne

City

Cambridgeshire

State

ZIP

CB3 6AA

Country

United Kingdom

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DECLARATION		ADDITIONAL INVENTOR(S) Supplemental Sheet Page 3 of 7	
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle if any)	Andrew James	Family Name or Surname	Flack
Inventor's Signature	<i>A. J. Flack</i>	Date	
Residence: City	Cambridgeshire	Country	United Kingdom
State		City	
ZIP	CB3 7XU	Country	United Kingdom
City	Cambridgeshire	State	
Country		City	
Address:	128 Lines Road Hardwick		
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle if any)	Christopher James Newton	Family Name or Surname	Fryer
Inventor's Signature	<i>C. J. Newton</i>	Date	7/6/02
Residence: City	Cambridge	Country	United Kingdom
State	GBX	City	
ZIP	CB4 8SD	Country	United Kingdom
City	Cambridge	State	
Country		City	
Address:	149, High Street Cottonham		
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle if any)	Jonathan Randall	Family Name or Surname	Garnsworthy
Inventor's Signature	<i>J. Randall</i>	Date	21 May 2002
Residence: City	Cambridge	Country	United Kingdom
State	GBX	City	
ZIP	CB1 2BW	Country	United Kingdom
City	Cambridge	State	
Country		City	
Address:	100 Tenison Road		
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle if any)	Ian Michael Daines	Family Name or Surname	Gaylor
Inventor's Signature	<i>I. Daines</i>	Date	
Residence: City	Cambridgeshire	Country	United Kingdom
State		City	
ZIP	CB3 5AA	Country	United Kingdom
City	Cambridgeshire	State	
Country		City	
Address:	24 Willow Lane Cambourne		

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ADDITIONAL INVENTOR(S)
Supplemental Sheet
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Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this assigned inventor	
Given Name (First and middle if any)		Family Name or Surname	
Andrew James		Flack	
Inventor's Signature		Date	
<i>A. J. Flack</i>			
Residence City		Country	Citizenship
Cambridgeshire		United Kingdom	United Kingdom
Mailing Address:			
128 Limes Road Hawdwick			
City		State	Country
Cambridgeshire		2P	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this assigned inventor	
Given Name (First and middle if any)		Family Name or Surname	
Christopher James Newton		Fryer	
Inventor's Signature		Date	
Residence City		Country	Citizenship
Cambridge		United Kingdom	United Kingdom
Mailing Address:			
149, High Street Cottenham			
City		State	Country
Cambridge		CB4 5SD	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this assigned inventor	
Given Name (First and middle if any)		Family Name or Surname	
Jonathan Randall		Gamsworthy	
Inventor's Signature		Date	
<i>J. Randall</i>		21 May 2002	
Residence City		Country	Citizenship
Cambridge		United Kingdom	United Kingdom
Mailing Address:			
100 Tenison Road			
City		State	Country
Cambridge		2P	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this assigned inventor	
Given Name (First and middle if any)		Family Name or Surname	
Ian Michael Daines		Gaylor	
Inventor's Signature		Date	
<i>Ian Gaylor</i>		6.6.02	
Residence City		Country	Citizenship
Cambridgeshire		United Kingdom	
Mailing Address:			
24 Willow Lane Cambsourne			
City		State	Country
Cambridgeshire		2P	United Kingdom

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ADDITIONAL INVENTOR(S)

Supplemental Sheet

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Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))	Richard J.	Family Name or Surname	Hammond
Inventor's Signature	<i>R. J. Hammond</i>	Date	21/5/02
Residence: City	Cambridge	State	GBK
	United Kingdom	Country	United Kingdom
Mailing Address:	16 Granta Terrace Great Shelford		
City	Cambridge	State	GBK
ZIP	CB2 5JD	Country	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))	John Robert	Family Name or Surname	Mc Garra
Inventor's Signature	<i>J. R. McGarra</i>	Date	20/5/02
Residence: City	Cambridge	State	GBK
	United Kingdom	Country	United Kingdom
Mailing Address:	331 Histon Road		
City	Cambridge	State	GBK
ZIP	CB4 3NF	Country	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))	Mike R.	Family Name or Surname	Nelson
Inventor's Signature	<i>M. Nelson</i>	Date	
Residence: City	Cambridgeshire	State	GBK
	United Kingdom	Country	United Kingdom
Mailing Address:	6 Field View Trinity Pastures, Bar Hill		
City	Cambridgeshire	State	GBK
ZIP	CB3 8SX	Country	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle (if any))	Oliver Alexander	Family Name or Surname	Shergold
Inventor's Signature		Date	
Residence: City	Cambridgeshire	State	GBK
	United Kingdom	Country	United Kingdom
Mailing Address:	51 High Street Cottenham		
City	Cambridgeshire	State	GBK
ZIP	CB4 4SA	Country	United Kingdom

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DECLARATION		ADDITIONAL INVENTORS Supplemental Sheet Page 6 of 7	
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle if any)	Richard J.	Family Name or Surname	Hammond
Inventor's Signature	<i>R. J. Hammond</i>	Date	21/5/02
Residence: City	Cambridge	Country	United Kingdom
Mailing Address:	16 Grants Terrace Great Shelford		
City	Cambridge	State	CB2 5JD
Country	United Kingdom	City	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle if any)	John Robert	Family Name or Surname	Mc Garra
Inventor's Signature	<i>J. R. Mc Garra</i>	Date	20/5/02
Residence: City	Cambridge	Country	United Kingdom
Mailing Address:	331 Histon Road		
City	Cambridge	State	CB4 3NF
Country	United Kingdom	City	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle if any)	Mike R.	Family Name or Surname	Nelson
Inventor's Signature	<i>M. Nelson</i>	Date	
Residence: City	Cambridgeshire	Country	United Kingdom
Mailing Address:	6 Field View Trinity Pastures, Bar Hill		
City	Cambridgeshire	State	CB3 8AX
Country	United Kingdom	City	United Kingdom
Name of Additional Joint Inventor, if any:		<input type="checkbox"/> A petition has been filed for this unsigned inventor	
Given Name (first and middle if any)	Oliver Alexander	Family Name or Surname	Shergold
Inventor's Signature	<i>O. Alexander</i>	Date	12/6/02
Residence: City	Cambridgeshire	Country	United Kingdom
Mailing Address:	51 High Street Cottonham		
City	Cambridgeshire	State	CB4 4SA
Country	United Kingdom	City	United Kingdom

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ADDITIONAL INVENTOR(S)

Supplemental Sheet

Page 7 of 7

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Richard Andrew

Family Name
or Surname

Snell

Inventor's
Signature

Cambridgeshire

Date

17 May 2002

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State

ZIP

CB1 4TY

Country

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Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Jake Philip

Family Name
or Surname

Turner

Inventor's
Signature

Cambridgeshire

Date

23/5/2002

Residence: City

State

GBR

United Kingdom

Country

Citizenship

Mailing
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Cottenham

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State

ZIP

CB4 8XX

Country

United Kingdom

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))

Eric

Family Name
or Surname

Wilkinson

Inventor's
Signature

Cambridgeshire

Date

23/5/02

Residence: City

State

GBR

United Kingdom

Country

Citizenship

Mailing
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Hilton

City

Cambridgeshire

State

ZIP

PE28 9PD

Country

United Kingdom

Name of Additional Joint Inventor, if any:

☐ A petition has been filed for this unsigned inventorGiven Name
(first and middle (if any))Family Name
or SurnameInventor's
Signature

Date

Residence: City

State

Country

Citizenship

Mailing
Address:

City

State

ZIP

Country